UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

MEMORANDUM & ORDER
MOTION FOR CLASS CERTIFICATION

----------X

In re: ZYPREXA PRODUCTS LIABILITY LITIGATION

04-MD-1596

----------X

UFCW LOCAL 1776 AND PARTICIPATING EMPLOYERS HEALTH AND WELFARE FUND, ERIC TAYAG, and MID-WEST NATIONAL LIFE INSURANCE COMPANY OF TENNESSEE, on behalf of themselves and others similarly situated,

05-CV-4115
05-CV-2948

Plaintiffs,

vs.

ELI LILLY AND COMPANY,

Defendant.

----------X

LOCAL 28 SHEET METAL WORKERS, on behalf of themselves and others similarly situated,

06-CV-0021

Plaintiffs,

vs.

ELI LILLY AND COMPANY,

Defendant.

----------X

SERGEANTS BENEVOLENT ASSOCIATION HEALTH AND WELFARE FUND, on behalf of themselves and others similarly situated,

06-CV-6322

Plaintiffs,

vs.

ELI LILLY AND COMPANY,

Defendant.

----------X

APPEARANCES:

For the Plaintiffs: HAGENS BERMAN SOBOL SHAPIRO LLP
One Main Street, 4th Floor
Cambridge, MA 02142
BY: THOMAS M. SOBOL
DAVID S. NALVEN

LAUREN G. BARNES
KRISTEN A. JOHNSON

HAGENS BERMAN SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900
Seattle, WA 98101
BY: STEVE W. BERMAN
CHRISTOPHER O'HARA

MURRAY LAW FIRM
650 Poydras Street, Suite 2150
New Orleans, LA 70130
BY: JAMES R. DUGAN, II
DOUG PLYMALE, PH. D.

KENNEY, EGAN, MCCAFFERTY & YOUNG
3031C Walton Road, Suite 202
Plymouth Meeting, PA 19462
BY: BRIAN P. KENNEY
ERIC L. YOUNG

HANLY CONROY BIERSTEIN SHERIDAN
FISHER & HAYES LLP
112 Madison Avenue
New York, NY 10016
BY: JAYNE CONROY
PAUL J. HANLY, JR.
ANDREA BIERSTEIN

SIMMONS COOPER, LLC
707 Berkshire Blvd.
P.O. Box 521
East Alton, IL 62024
BY: TOR A. HOERMAN
GREG ERTHEAL

ZIMMERMAN REED PLLP
651 Nicollet Mall, Suite 501
Minneapolis, MN 55042
BY: RONALD S. GOLDSER
STACY K. HAUER
BRIAN C. GUDMUNDSON

IVEY & RAGSDALE
315 West 19th Street
Jasper, AL 35501-5323
BY: GARVE IVEY
BARRY RAGSDALE

CHARFOOS & CHRISTENSEN PC
5510 Woodward Avenue
Detroit, Michigan 48202

BY: ANN MANDT
DAVE PARKER

J. THOMPSON & ASSOCIATES LLC
26000 W. Twelve Mile Road
Southfield, MI 48034
BY: JASON J. THOMPSON

CHRISTOPHER A. NEAL & ASSOCIATES
300 Harwood
Bedford, TX 76021
BY: CHRISTOPHER A. NEAL

KAHN GAUTHIER LAW GROUP, L.L.C
650 Poydras Street, Suite 2150
New Orleans, LA 70130
BY: LEWIS KAHN
ERIC O'BELL

MURRAY LAW FIRM
909 Poydras Street, Suite 2550
New Orleans, LA 70112-4000
BY: STEPHEN B. MURRAY, SR.
STEPHEN MURRAY, JR.

SADIN LAW FIRM, P.C.
121 Magnolia, Suite 102
Friendswood, TX 77546
BY: ART SADIN

HARKE & CLASBY LLP
155 South Miami Avenue Suite 600
Miami, Florida 33130
BY: LANCE A. HARKE
HOWARD M. BUSHMAN

For the Defendant:

PEPPER HAMILTON, LLP
3000 Two Logan Square
Eighteenth & Arch Sts.
Philadelphia, Pennsylvania 19103
BY: NINA M. GUSSAK
THOMAS E. ZEMAITIS
ANTHONY VALE
ADAM B. MICHAELS
KENNETH J. GRUNFELD
PAUL V. AVELAR

PEPPER HAMILTON, LLP
620 Eighth Avenue
37th Floor
New York, NY 10018-1405
BY: SAMUEL J. ABATE, JR.

JACK B. WEINSTEIN, Senior United States District Judge:

Table of Contents

I. Introduction

A. Overview

Institutions and individuals sue on behalf of a class for overpayment on purchases of defendant Eli Lilly and Company's ("Lilly") antipsychotic prescription drug Zyprexa. Institutional plaintiffs are third-party payors ("TPPs") such as pension funds, labor unions, and insurance companies. They cover members' health benefits; they have paid for Zyprexa, as well as many other pharmaceuticals upon which people rely. Individual plaintiffs bought or paid a portion of the purchase price for Zyprexa for their own use.

Claimed is a substantive violation of the Racketeer Influenced and Corrupt Organizations Act ("RICO") through mail fraud, predicated on overpricing supported by excessive claims of

utility as well as disavowal of adverse secondary effects of the drug, primarily weight gain and diabetes. *See* 18 U.S.C. § 1964.

There is sufficient evidence of fraud under RICO to go to a jury. Proposed testimony of plaintiffs' experts would permit a jury to determine the excess price. Allocation of damages based on that excess, predicated on written receipts and other reliable information, is practicable. For the institutional plaintiffs' RICO claims, every element of Rule 23 of the Federal Rules of Civil Procedure has been satisfied. *See* Part XX, *infra*. Certification of these TPP claims is appropriate under federal substantive law.

Certification of individual payor claims is denied. It will be difficult to obtain the necessary reliable payment data in most cases. More important, the individual plaintiffs proposed as representatives cannot properly represent the proposed class of individual persons. They have a conflict of interest since they are suing Lilly for personal injury and could potentially sacrifice the proposed overpayment class for a better recovery in their related individual suits. Separate releases for the two claims do not overcome this conflict. *See* Aff. of Douglas R. Plymale 3, June 23, 2008, Docket No. 05-CV-4115, Docket Entry No. 197; Parts II.A.2.a.iv, II.A.2.b.iv, XIX.B, *infra*. In any event, even if the individual plaintiffs were to be certified as a subclass, their separate counsel (needed to avoid ethical problems of conflicts) and different issues of proof would unduly complicate the trial. Were the case to be settled, the claims of individuals as well as of other possible plaintiffs, such as the United States and state attorneys general, could be folded into one class with subclasses. *See, e.g.*, Hr'g Tr., July 17, 2008.

State-based claims for a recovery are also made. No ruling on the certificability of those claims will be made at this time. Under the particular circumstances of this case, the state causes

of action would essentially be subsumed in the single federal RICO action. As certified for litigation purposes, state-based substantive claims are excluded. Were the case to be settled, inclusion as part of the settlement would be desirable to help bring the total litigation to closure and to avoid future claims. *See* Parts XIX.A.2, XIX.C, XXI.B, *infra*.

A single price was charged for uses of the drug approved by the United States Food and Drug Administration ("FDA") ("on-label") and those not so approved ("off-label"). Subclassing for these two categories of drug use is proposed, but is denied. There is evidence that off-label use of Zyprexa was excessive and may have been encouraged by Lilly. *See, e.g.*, Laurie Tarkan, *Doctors Say Medication* [*Including Zyprexa*] *Is Overused in Dementia,* N.Y. Times, June 24, 2008, at F1. A cause of action for Lilly's urging such off-label use may exist, but it is independent of the case as it is now being certified based solely on overcharging for use of Zyprexa in any form. Subclassing of on-label and off-label purchases can be reconsidered were there a total settlement. *See* Parts XIX.A.1.c-d, *infra*.

Damages sought are limited to four years before filing. No damages will be allowed beyond the initial complaint's filing date of June 20, 2005. By then all potential third-party payors and prescribers of Zyprexa should have been sufficiently aware of the alleged overpricing, especially considering the widespread publication that year of adverse clinical trial results. As a matter of substantive equity, no damages will be allowed before June 20, 2001, four years before the suit was commenced. Permitting recovery for overcharges before that date would be inappropriate since the specialists who are the third-party payors had a continuing duty to their clients to inquire and to be aware of the value of drugs for which they were paying. In these special circumstances, limits should be placed on losses attributable to plaintiffs' passivity.

This ruling will result in a maximum period of June 20, 2001 to June 20, 2005 for recoverable overcharges. A jury may reduce, or even eliminate, this window on finding that the third-party payors knew or should have known of Zyprexa's alleged overpricing before they commenced suit on June 20, 2005. This limitation on the recovery period by the court depends upon exercise of the court's discretion. *See* Part XX.B.4, *infra*.

The parties have proposed slightly different certification orders, including the definition of the class, and have agreed on the parameters of the plan of notice. *See* Pfs.' Proposed Order on Class Cert. attach. 1, Aug. 22, 2008, Docket Entry No. 227; Def.'s Proposed Order, Aug. 22, 2008, Docket Entry No.228 Ex. 1; *see* Part XXIV, *infra*. Defendant opposes any certification but has cooperated in providing appropriate forms of orders.

An interlocutory appeal is now certified on this court's order denying summary judgment. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571 (E.D.N.Y. 2007) (denying motion for summary judgment). Interlocutory appeal provisions of Rule 23(f) of the Federal Rules of Civil Procedure on certification of the class also apply. *See* Fed. R. Civ. P. 23(f). Further proceedings in this court are now stayed in the class action certified, *see* Part XXIII, *infra*; related Zyprexa actions not encompassed in this certified action may go forward. *See* Part I.C, *infra*. So, too, may the unsealing process. *See* Part II.C, *infra*.

Details on methods of administration of the litigation, beyond those outlined in this memorandum, appropriately await proceedings after a possible interlocutory decision by the Court of Appeals for the Second Circuit. No substantial difficulty in providing for the particulars of administrating this class action litigation is foreseen. Federal courts have handled class actions far more complex than this one with a relative ease of administration. *See* Part XXII,

infra. Despite its theoretical substantive and procedural simplicity, the case comes freighted with complex medical details, economic models, and important implications for our national health care system.

Allocation of scarce medical resources is reflected in large part by the cost of medications doctors prescribe. Drugs are primarily paid for by third-party payors rather than by the doctors who recommend them or the patients who use them. *See, e.g.*, Peter H. Schuck & Richard J. Zeckhouser, Targeting in Social Programs 56-57 (2006) ("[P]olicymakers and plan managers are relying on physicians to be vigilant stewards of scarce resources," even though they are often ineffective in controlling costs). TPPs include insurance funds and other health management organizations ("HMOs") such as the plaintiffs in the instant action. These screeners of drug use must have reasonably accurate and transparent sources of information if they are to make reasonable medical and economic choices. So too must doctors and their patients.

The FDA is expected to guard the quality of available information about the utility and risks of pharmaceuticals by regulating drug approvals and labeling requirements, monitoring adverse side effects, and requiring warnings and "Dear Doctor" letters. Non-governmental agencies, individual expert research, publications, meetings, and word-of-mouth supply an enormous amount of additional data on which doctors and other screeners of drug use rely. Tort law has an important function in guarding against the pollution of information the medical calling and patients receive, particularly since our federal agency, the FDA, is relatively impotent in protecting against misleading by drug manufacturers.

Sold under the brand name Zyprexa, olanzapine is one of a class of medications known as "atypical" or "second-generation" antipsychotics ("SGAs"). (This memorandum uses "Zyprexa"

and "olanzapine" interchangeably.) It is a prescription drug developed and manufactured by Lilly. The FDA first approved Zyprexa in 1996 for use in treating schizophrenia, a severe mental illness; Zyprexa was later approved for treating some types of bipolar disorders and other diseases. Olanzapine's main adverse side effects appear to be weight gain, diabetes, hyperglycemia, and other metabolic problems.

Zyprexa continues to be used by, and prescribed for, large numbers of people. There is a general consensus that it is useful for both FDA-approved indications and some off-label purposes. It has substantially increased the quality of life of some sufferers from severe mental problems. *See, e.g.*, Elyn R. Saks, The Center Cannot Hold: My Journey Through Madness 303 (2008) ("I began to take Zyprexa . . . . The change was fast and dramatic. . . . I felt alert and rested, energetic in a way I hadn't felt in a long time—so long, in fact, that I'd almost forgotten what those good feelings were like. . . . The clinical result was, not to overstate it, like daylight dawning after a long night—I could see the world in a way I'd never seen it before.").

Beneficial effects of Zyprexa are evidenced by the fact that the institutional plaintiffs continue to reimburse or pay for Zyprexa prescriptions for their members, with few or no restrictions on its use. Many treating physicians prescribe it for their patients, despite its now well-known metabolic side effects. Nevertheless, the utility of Zyprexa does not trump plaintiffs' legal claims for fraud and overpricing.

B. Plaintiffs' Claims

Plaintiffs claim overpayment through direct expenditures for Zyprexa. Individual patients buy Zyprexa for personal use pursuant to the prescriptions of their doctors, paying the full, or a portion of, market price according to particular insurance plans. Third-party payors pay the

remainder for their covered members, typically via pharmaceutical benefit managers ("PBMs"), which act as TPP agents in administering their prescription drug programs.

It is alleged that over the twelve-year period since Zyprexa's introduction in 1996 to today, Lilly has withheld information and disseminated misinformation about the safety and efficacy of Zyprexa and has promoted and marketed the drug for uses for which it was not indicated and for patients who would have been better served by less expensive medications. As a result, plaintiffs contend, Zyprexa commanded a higher price than it would have had the truth been known to those who prescribed, bought, or paid for the drug. The resulting alleged excess payments—estimated to range from $3.998 billion to $7.675 billion (per plaintiffs' expert Dr. Rosenthal) or to approximate $4.9 billion (per plaintiffs' expert Dr. Harris)—are claimed as damages. *See* Parts XVIII.A.2-3, *infra*. Having survived summary judgment, *see In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, plaintiffs now seek certification of a class of third-party and individual payors.

Five causes of action are asserted: Counts I and II, violations of the Racketeer Influenced and Corrupt Organization Act ("RICO") under 18 U.S.C. §§ 1962(c) and 1962(d); Count III, violations of forty-five state consumer protection statutes; Count IV, common law fraud; and Count V, unjust enrichment. *See* First Am. Class Action Compl. (Redacted), Nov. 7, 2005, Docket No. 05-CV-4115, Docket Entry No. 14 ("Am. Compl").

Subject matter jurisdiction is based upon 28 U.S.C. § 1331 (action arising under the laws of the United States) and 18 U.S.C. §§ 1962 and 1964(c) (RICO). Plaintiffs also invoke jurisdiction pursuant to 28 U.S.C. § 1332(d)(2) ("Class Action Fairness Act"). Venue is placed in the Eastern District of New York pursuant to 28 U.S.C. § 1391(b) and (c) (requiring that a

substantial portion of the alleged improper conduct took place in the district where suit is commenced) and 18 U.S.C. § 1965 (RICO). As already noted, claims under Counts III, IV and V are not being certified.

C. Related Actions

Related Zyprexa actions provide the court and litigants with an extensive factual and evidentiary background. The present suit is part of a series of cases based on injuries allegedly resulting from Lilly's sale of Zyprexa. Thousands of mass tort product liability personal injury actions against Lilly on behalf of approximately 30,000 private litigants have been transferred to this court by the Judicial Panel on Multidistrict Litigation ("JPML") since April 2004; almost all of them have now settled. *See* JPML Order, *In re Zyprexa Prods. Liab. Litig.*, No. 04-CV-1596, Docket Entry No. 1 (E.D.N.Y.); 28 U.S.C. § 1407. The large number of related individual personal injury suits necessitated administration of the multidistrict litigation ("MDL") as a quasi-class action, with the use of matrices for settlement amounts, control over fees, cooperation with state courts and national settlements of liens. *See In re Zyprexa Prods. Liab. Litig.*, 451 F. Supp. 2d 458, 477 (E.D.N.Y. 2006) (recognizing the court's "obligation to exercise careful oversight of this national 'quasi-class action'") (citation omitted); *In re Zyprexa Prods. Liab. Litig.*, 433 F. Supp. 2d 268, 271 (E.D.N.Y. 2006) (finding that the case "may be characterized properly as a quasi-class action subject to the general equitable power of the court"); *In re Zyprexa Prods. Liab. Litig.*, 424 F. Supp. 2d 488, 491 (E.D.N.Y. 2006) (same); *In re Zyprexa Prods. Liab. Litig.*, 233 F.R.D. 122, 122 (E.D.N.Y. 2006) (same).

Various administrative measures were taken to control discovery and ensure appropriate representation for the personal injury plaintiffs. Two successive Plaintiffs' Steering Committees

("PSCs") were appointed. *See* Case Mgmt. Order No. 19, Aug. 16, 2006, Docket No. 04-MD-0159, Docket Entry No. 692; *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2004 WL 3520245 (E.D.N.Y. June 17, 2004) (outlining the PSC's responsibilities). Multiple special masters and a magistrate judge assisted.

Extensive and coordinated discovery led to creation of a national archive available to all parties. *See In re Zyprexa*, 424 F. Supp. 2d at 491 ("[A]ll litigants, whether in federal or any state court, have access to the materials obtained in pretrial discovery"). Those documents, including depositions, are available to the parties in the instant class action. The collection, maintained initially in a depository in Denver, Colorado, and currently in Mount Pleasant, South Carolina, has been available free of charge to the MDL and non-MDL plaintiffs in both state and federal courts who agree to adhere to the terms of the protective and related orders issued by this court. *See also* Case Mgmt. Order No. 20 at 1, Nov. 16, 2006, Docket No. 04-MD-1596, Docket Entry No. 928 (ordering special master's discovery and trial schedule for personal injury actions); *In re Zyprexa Prods. Liab. Litig.*, 375 F. Supp. 2d 190, 191 (E.D.N.Y. 2005); Case Mgmt. Order No. 15 at 5, May 15, 2006, Docket No. 04-MD-1596, Docket Entry No. 527 (directing MDL counsel to use best efforts to coordinate the scheduling of depositions with state court counsel, and providing for cross-noticing of depositions in federal and state court).

Because many of the personal injury suits were filed in state courts, coordination with state judges was desirable. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2006 WL 898105, at *1 (E.D.N.Y. Apr. 16, 2006) ("Coordination and cooperation between state and federal courts has been encouraged."); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2006 WL 197151 (E.D.N.Y. Jan. 30, 2006) (suggesting coordination and cooperation in a letter

to state judges with Zyprexa cases); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2004 WL 3520248, at *4 (E.D.N.Y. Aug. 18, 2004) (directing Lilly and the first PSC ("PSC I") to "confer regarding procedures for coordination of state court discovery with discovery in this MDL").

Over 8,000 personal injury claims, representing about 75% of the then-pending plaintiffs, were settled by Lilly in 2005 under the supervision of PSC I. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2005 WL 3117302 (E.D.N.Y. Nov. 22, 2005). A complex claims processing and payment procedure was established, administered via special settlement masters. *See In re Zyprexa Prods. Liab. Litig.*, 433 F. Supp. 2d 269 (E.D.N.Y. 2006); *see also In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2443217 (E.D.N.Y. Aug. 24, 2006) (ordering payments to begin); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2443249 (E.D.N.Y. Aug. 24, 2006) (establishing disbursement procedures). Another 18,000 such plaintiffs settled with Lilly in January 2007; settlement was largely administered by an appointed settlement administrator rather than the court. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-CV-1596, 2007 WL 37736 (E.D.N.Y. Jan. 5, 2007). Since then, many more plaintiffs have settled or agreed to settle. *See, e.g.*, *In re Zyprexa Prods. Liab. Litig.*, No. 04-CV-1596, 2008 WL 1827486 (E.D.N.Y. Apr. 22, 2008) (ordering the administrative closure of over a thousand cases pending reinstatement should the contemplated settlements not be consummated).

Summary judgment motions in several individual plaintiffs' personal injury claims were addressed in June 2007. Analysis of the summary judgment motions required review of thousands of pages of material. *See* Appendices A-D of *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230 (E.D.N.Y. 2007) (including over 1500 pages of relevant depositions demonstrating

doctors' awareness of Zyprexa's association with patient weight gain). In one claim, defendant's motion was granted based on statute of limitations grounds. *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230. Other personal injury lawsuits set for trial in this district in June 2008 were settled before summary judgment could be rendered. *See, e.g.*, *Godley v. Eli Lilly & Co.*, Docket No. 06-CV-04038 (E.D.N.Y.); *Smith v. Eli Lilly & Co.*, Docket No. 06-CV-04039 (E.D.N.Y.).

For the personal injury settlements, an attorneys' fees structure was ordered. *See In re Zyprexa Prods. Liab. Litig.*, 424 F. Supp. 2d 488 (capping fees at 20% of recovery for smaller, lump-sum claims, and at 35% for all other claims); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2006 WL 2443248 (E.D.N.Y. Aug. 24, 2006) (limiting PSC costs charged to the individual settling plaintiffs); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2006 WL 2458878 (E.D.N.Y. Aug. 22, 2006) (referring oversight of PSC I's fee claims to the magistrate judge).

Cases commenced in this district are being prepared for trial here in clusters of twelve. *See* Case Mgmt. Order Nos. 29, 30, Aug. 19, 2008, Docket No. 04-MD-1596, Docket Entry Nos. 1838, 1840. The expectation is that all will be tried, dismissed or settled by the spring of 2009. *See* Hr'g Tr., Aug. 11, 2008. Cases transferred from other districts will have general discovery completed at about the same time, when transfer will be suggested for the relatively few that have not been settled or dismissed. *See* Case Mgmt. Order No. 28, July 11, 2008, Docket No. 04-MD-1596, Docket Entry No. 1796.

Since many of the personal injury plaintiffs had coverage for health-related expenditures through state Medicaid and federal Medicare programs, a procedure for resolving outstanding government liens was executed. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006

WL 2385230 (E.D.N.Y. Aug. 15, 2006) (describing and approving Medicaid lien agreements between states and the PSC); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2385232 (E.D.N.Y. Aug. 16, 2006) (describing fee division issues); *In re Zyprexa Prods. Liab. Litig.*, 451 F. Supp. 2d 458 (creating a national mechanism to resolve outstanding Medicare and Medicaid liens on the recoveries of settling personal injury plaintiffs); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2006 WL 3501263, at *1 (E.D.N.Y. Dec. 4, 2006) ("In compliance with this court's instructions . . . all fifty states as well as the federal government have resolved their Medicare and Medicaid liens" by agreeing to modify their lien demands to provide a national equitable system) (citation omitted); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2443217 (E.D.N.Y. Aug. 24, 2006) (describing and approving Medicare lien agreements between certain states, the federal government, and the PSC); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2385230 (E.D.N.Y. Aug. 15, 2006) (same); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2095728 (E.D.N.Y. July 28, 2006) (ordering Lilly and the states to negotiate); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 1662610 (E.D.N.Y. June 15, 2006) (setting initial conference regarding a possible holdback to satisfy government liens).

Non-governmental health insurance liens were dealt with on an individual basis. A private health insurance company sued the trustees of the first Zyprexa settlement fund for failure to resolve such liens; that matter has now been settled. *See Aetna, Inc. v. Seeger Weiss, LLP*, No. 07-CV-03559 (E.D.N.Y.).

In suits based on claims similar to those in the instant action, many state attorneys general have sued on behalf of their states' citizens claiming reimbursement for overpayments for

Zyprexa made with state and federal funds via state Medicaid programs. Currently pending in this court are actions on behalf of the citizens of Montana, Connecticut, New Mexico, Mississippi, West Virginia, and Louisiana. *See In re Zyprexa Prods. Liab. Litig.*, No. 07-CV-1933, 2008 WL 398378 (E.D.N.Y. Feb. 12, 2008) (Montana, denying remand); *Hood ex rel. Mississippi v. Eli Lilly & Co.*, No. 07-CV-645, 2007 WL 1601482 (E.D.N.Y. June 5, 2007) (Mississippi, denying remand); *In Zyprexa Prods. Liab. Litig.*, 375 F. Supp. 2d 170 (E.D.N.Y. 2005) (Louisiana, denying remand); *West Virginia v. Eli Lilly & Co.*, 476 F. Supp. 2d 230 (E.D.N.Y. 2007) (West Virginia, denying remand); *Connecticut v. Eli Lilly & Co.*, No. 08-CV-955 (E.D.N.Y.); *In re Zyprexa Prods. Liab. Litig.*, No. 07-CV-1749, 2008 WL 940102 (E.D.N.Y. Apr. 1, 2008) (New Mexico, scheduling discovery); *cf.* Alex Berenson, *Lilly Considers $1 Billion Fine to Settle Case*, N.Y. Times, Jan. 31, 2008 (federal and state negotiations with Lilly over a proposed fine). A putative qui tam action by a whistleblower representing California has been dismissed. Order, *California ex rel. Jaydeen Vincente v. Eli Lilly & Co.*, Apr. 23, 2008, Docket No. 08-CV-600, Docket Entry No. 84 (dismissing action). A number of state attorney general cases are pending in state courts. *See* Hr'g Tr., Aug. 11, 2008 (five cases). The one case originating in this district, that of Connecticut, will be tried on June 15, 2009 if it has not been settled or dismissed. *See* Order, Aug. 11, 2008, Docket No. 04-MD-1596, Docket Entry No. 1828. It is expected that by the summer of 2009, the five attorney general cases transferred to this court will have been settled, dismissed, or, with general discovery completed, transferred back to their originating jurisdictions. *Id.*

Some of Lilly's shareholders have filed suit because of the decline in share price. *See In re Eli Lilly & Co. Securities Litig.*, No. 07-CV-1310 (E.D.N.Y.). This litigation has been

dismissed on statute of limitations grounds. *See In re Zyprexa Prods. Liab. Litig.*, 549 F. Supp. 2d 496 (E.D.N.Y. 2008).

Current shareholders have sued in this court in the form of three separate shareholder derivative actions. *See Waldman v. Taurel*, No. 08-CV-560 (E.D.N.Y.); *City of Taylor Employees Retirement System v. Taurel*, No. 08-CV-1554 (E.D.N.Y.); *Robins v. Taurel*, No. 08-CV-1471 (E.D.N.Y.). Similar cases are pending in other courts. Settlement negotiations are ongoing. *See* Hr'g Tr., May 29, 2008.

The present suit must be considered in the context of the related Zyprexa actions. Materials previously submitted to the court in the MDL were, on consent of the parties, considered in deciding this class certification motion. *See* Transcript of Evidentiary Proceedings on Class Certification, March 28, 2008 through April 2, 2008 ("Tr."), at 5-6 (Mar. 28, 2008). Materials from the parties' previous summary judgment motions, *see In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, are extensively cited.

In March 2008, Lilly settled with the state of Alaska for $15 million during trial in a related case. *See* Alex Berenson, *Lilly Settles Alaska Suit over Zyprexa*, N.Y. Times, Mar. 26, 2008 (reporting the settlement agreement reached after three weeks of trial before the case went to the jury). That state's lawsuit sought reimbursement for the medical costs of Alaska Medicaid patients who developed diabetes while taking Zyprexa; the state's claim to recover costs associated with Lilly's off-label promotion of Zyprexa was dismissed before trial. Alex Berenson, *Lilly E-Mail Discussed Off-Label Drug Use*, N.Y. Times, Mar. 14, 2008. Some of the materials introduced in that trial are available in this court.

D. Class Certification

Plaintiffs seek to consolidate many thousands of claims in the present class action on the ground that those who paid for Zyprexa were charged more than they would have been in the absence of Lilly's fraud. Claims include those of both patients and insurance companies. Various definitions of the putative class have been proposed. As outlined in plaintiffs' papers, the class may be generally defined as:

> All individuals and [non-governmental] entities in the United States and its territories who, for purposes other than resale, purchased, reimbursed, and/or paid for Zyprexa during the period from September 1996 through the present. For purposes of the Class definition, individuals and entities "purchased" Zyprexa if they paid for some or all of the purchase price.

Pfs.' Corr. Supp. Post-Hr'g Mem. on Class Cert. 32, Apr. 21, 2008 (undocketed; filed under seal); *see* Red. Am. Compl.; Class Plaintiffs' Opening Brief on Class Certification ("Pfs.' Class Cert. Br."), Aug. 3, 2007, Docket No. 05-CV-4115, Docket Entry No. 131 (filed under seal).

Two subclasses are proposed: a Third-Party Payor Subclass and a Consumer or Direct-Payor Subclass. Further division into two groups, one for "on-label" (used for FDA-approved indications) purchases and the other for "off-label" (used for non FDA-approved indications) purchases has also been suggested by plaintiffs. Pfs.' Corr. Supp. Post-Hr'g Mem. on Class Cert. 33; *see* Fed. R. Civ. P. 23(c)(5); Part XIX.A, *infra*.

The class will be certified on a more limited basis than that sought by plaintiffs. *See* Part XXI, *infra*. With adequate due process protections for both plaintiffs and defendant, restrictions on the litigation will permit the jury to determine, with sufficient precision, the monetary damages, if any, to institutions that allegedly overpaid for Zyprexa as a result of Lilly's fraud. The assistance of *Daubert*-cleared experts and a plan for efficiently managing the litigation as a

class action, as opposed to individual suits, provide substantial benefits to the community and the courts and litigants.

Certification will be granted to a class of third-party payors on the federal RICO claims only. *See also In re Zyprexa Prod. Liab. Litig.*, 493 F. Supp. 2d 571, 577, 579 ("Based on expert reports and available modes of economic analysis, a trier could determine that Zyprexa would have . . . been sold for a reasonably precise computable lesser amount than it was sold for were it not for Lilly's alleged fraud."). Plaintiffs' state claims will not be certified at this time by this court.

Establishment of class damages is practicable based upon the admissible opinions of plaintiffs' proffered experts. In these circumstances the Constitution requires a jury disposition. *See* U.S. Const. amend. VII. For purposes of the constitutional right to a civil jury, this is essentially a "suit at common law," even though plaintiffs rely on statutory substantive law and equitable class action practice. *See* Part XIX.D, *infra*.

Total denial of certification would constitute the death knell of the action. Almost all plaintiffs' claims would be too small to individually support this costly litigation. Under such circumstances, absent an unusual situation, the rule to be applied in deciding to deny certification is essentially that for summary judgment if all the elements of Rule 23 of the Federal Rules of Civil Procedure are satisfied—as they are here. *See* Fed. R. Civ. Proc. 23; Part XX, *infra*.

In arguing against class certification, defendant relies heavily on the Second Circuit Court of Appeals' reversal of *Schwab v. Philip Morris*, 449 F. Supp. 2d 992 (E.D.N.Y. 2006), in *McLaughlin v. American Tobacco Co.*, 522 F.3d 215 (2d Cir. 2008), *subsequently placed in doubt by Bridge v. Phoenix Bond & Indemnity Co.*, 128 S. Ct. 2131 (2008). Denial of some

aspects of defendant's motion for summary judgment was based in part on *Schwab*. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571. The instant action and that in *McLaughlin* superficially may appear alike: in both, consumers have sued for overpricing based on fraudulent health claims of the product—medication or cigarettes. *McLaughlin* is, as explained below, distinguishable from the present case. Assuming *McLaughlin* is still fully viable in view of the subsequent Supreme Court decision in *Phoenix Bond* expanding the reach of civil RICO actions, it is not an impediment to certification in the instant Zyprexa case. *See* Parts XX.B-D, *infra*.

E. Opportunity to Comment

Due to the enormous number of potential plaintiffs involved and the importance of the case, the court made a special effort to solicit and to incorporate in this memorandum and order the views of those who might be interested. To this end, the court issued a "Discussion Draft" of this class certification memorandum several months ago. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-CV-4115, 2008 WL 2696916 (E.D.N.Y. June 2, 2008). Comments of interested persons or parties were solicited for a subsequent hearing on class certification:

> Because the class proposed to be certified in the draft opinion specifically excludes government and individual payors, the United States Attorney or other representative of the federal government, state Attorneys General or equivalent state officials, or any individual or representative of an interested group will be heard if so desired. Testimony at the previously held certification hearings related to government and individual payments, as well as to the activities of individual non-governmental organizations such as the American Diabetes Association and the National Alliance on Mental Illness.

In re Zyprexa Prods. Liab. Litig., No. 05-CV-4115, 2008 WL 2779068 (E.D.N.Y. July 14, 2008); Hr'g Tr., July 17, 2008; Oral Statement by the Court at Class Cert. Hr'g, July 17, 2008, Docket No. 05-CV-4115, Docket Entry No. 207; Order, July 17, 2008, Docket Entry No. 208.

Interested parties or persons were invited to participate in the court's September 4, 2008 hearing on the motions to unseal Lilly documents, until then confidential pursuant to a long-standing protective order. *See In re Zyprexa Prods. Liab. Litig.*, No. 05-CV-4115, 2008 WL 3245091 (E.D.N.Y. Aug. 6, 2008); Letter, Bloomberg L.P., Aug. 18, 2008, Docket No. 05-CV-1596, Docket Entry No. 1832; Mot. to Vacate CMO 3, Vera Sharav, Alliance for Human Research Protection & David Cohen, Docket No. 04-MD-1496, Docket Entry No. 1859; Letter, Kaiser Health Foundation Plan et al., Aug. 22, 2008, Docket No. 04-MD-1496, Docket Entry No. 1847. Although the court's efforts towards public participation may have somewhat delayed the proceedings, the opportunity to reflect and provide for public comment seems more important than speed in this instance. The court postponed issuance of this final order of certification in order to consider the public and private interests reflected in the comments and motions it has received.

F. Interlocutory Appeal

As suggested in the summary judgment opinion, *see In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d at 580-81, an interlocutory appeal from the order denying summary judgment should be, and is now, certified. *See* Part XXIII, *infra*. This will permit that issue to be considered along with any immediate appeal from the class certification order. 28 U.S.C. § 1292(b); Fed. R. Civ. Proc. 23(f).

II. Procedural History

A. Multiple Plaintiffs

1. Third-Party Payor Plaintiffs

On June 20, 2005, Mid-West National Life Insurance Company of Tennessee ("Mid-West") and Eric Tayag ("Tayag") filed a putative class action suit against defendant Eli Lilly and Company ("Lilly") regarding the alleged fraudulent over-promotion of olanzapine, sold under the brand name Zyprexa, and seeking economic damages. *See* Mid-West & Tayag Compl., June 20, 2005, Docket No. 05-CV-2948, Docket Entry No. 1. Similar suits were initiated by UFCW Local 1776 and Participating Employers Health and Welfare Fund ("UFCW"), *see* UFCW Compl., Aug. 25, 2005, Docket No. 05-CV-4115, Docket Entry No. 1, Local 28 Sheet Metal Workers ("Local 28"), *see* Local 28 Compl. (Redacted Version), Dec. 29, 2006, Docket No. 06-CV-21, Docket Entry No. 1, and Sergeants Benevolent Association Health and Welfare Fund ("SBA"), *see* SBA Compl., Nov. 21, 2006, Docket No. 06-CV-6322, Docket Entry No. 1. The United Federation of Teachers Welfare Fund ("Teachers") and ASFCME District Council 37 Health and Security Fund ("DC 37") later joined as additional class representatives. In the fall of 2006, Michael Pronto ("Pronto") and Michael Vannello ("Vannello") were added as co-lead individual plaintiffs and Tayag was dropped as a class representative.

In response to Lilly's September 29, 2005 motion for an order requiring the filing of a RICO case statement, Def.'s Mot. for Order Requiring Plaintiff to File RICO Case Statement, Sept. 29, 2005, Docket No. 05-CV-4115, Docket Entry No. 8, plaintiffs filed an amended complaint on November 7, 2005, alleging in great detail Lilly's misrepresentations and fraudulent over-promotion. First Am. Class Action Compl. & Demand for Jury Trial, Nov. 7, 2005, Docket Entry No. 14.

a. UFCW

The UFCW Fund is a Taft-Hartley trust fund created to provide cost effective, comprehensive medical and prescription drug benefits to the Local 1776 members of the United Food & Commercial Workers Union ("UFCW Local 1776"), whose employers are required to contribute financially pursuant to negotiated union contracts. *See generally* 29 U.S.C. §§ 141-197 *et seq*. (Taft-Hartley Act, i.e., enabling federal law pursuant to which the UFCW Fund was created). UFCW Local 1776 is a labor union based in Philadelphia, Pennsylvania, with over 20,000 active members, some of whom live in other states. Pfs.' Class Cert. Br. Typical of Taft-Hartley benefit trust funds, the UFCW Fund has no employees. Dep. Tr. of Regina Reardon on behalf of Plaintiff UFCW, Oct. 5, 2006, at 15 ("UFCW Dep."). Since 1996, the UFCW Fund has contracted with a third-party administrator that collects employer contributions, maintains records, pays claims, and conducts the day-to-day operations of the UFCW Fund. *Id.* at 16. It has overall annual expenditures of $70 million, an increase of almost fifty percent over the last five years. *Id.* at 172-73.

Like most other third-party payors, the UFCW Fund, with the assistance of its third-party administrator, contracts with a Pharmacy Benefit Manager ("PBM") to manage its pharmacy plan. *Id.* at 16. The UFCW Fund pays for eligible Zyprexa prescriptions directly through its PBM, currently National Medical Health Card ("NMHC"). *Id.* at 86, 39. To manage the UFCW Fund's pharmacy benefits, NMHC uses a formulary containing a list of preferred drugs. Many of the drugs on the preferred list are those for which the NMHC has rebate contracts with the manufacturers. *Id.* at 91. The UFCW Fund pays the cost, minus a co-pay, regardless of whether the drug is included in the formulary. *Id.* at 84. The co-pay is a percentage of the drug cost or a fixed amount per prescription paid by the actual user; it may vary depending on whether the

particular drug is on-formulary or off-formulary. *Id.* at 99. UFCW has no direct means of determining the indication for which a prescription is written and whether it is for an on-label or off-label purpose. On May 15, 2007, UFCW's PBM formally recommended that the fund impose a prior authorization requirement for all Zyprexa prescriptions to discourage potential off-label use of the drug.

UFCW alleges that it has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. Am. Compl. at ¶¶ 472, 480, 535, 54, 546. It asserts that every Zyprexa prescription for which it has paid was procured by Lilly's fraud, Opp'n to Eli Lilly & Co.'s Mot. to Compel Further Resps. by Pfs. to Interrogs. & Doc. Reqs. & to Compel Mid-West's Rule 30(B)(6) Witness to Answer Questions, Dec. 1, 2006 ("Opp'n to Mot. to Compel") at 7, and has produced such Zyprexa prescription information as cost, dose and date.

From January 1997 through January 2006, the UFCW Fund paid a total of $799,888.16 for Zyprexa. Between January 31, 1997 and April 10, 1997, it paid for 5,514 units; between June 9, 1999 and January 11, 2002, it paid for 3,226 units; between June 4, 2003 and June 16, 2003, it paid for 1,345 units; and between December 12, 2003 and January 5, 2006, it paid for 57,569 units. UFCW used various PBMs between 1996 and 2000; since not all of them maintained data on Zyprexa, there are some gaps in the records.

According to plaintiffs, Lilly sales representative call notes produced in discovery suggest that several physicians who prescribed Zyprexa to the UFCW Fund's insureds were deceived by Lilly before, or while, prescribing Zyprexa. Pfs.' Response to Def.'s Local R. 56.1 Statement of Undisputed Facts & Pfs.' Local R. 56.1 Statement of Disputed Facts, June 12, 2007, Docket No.

05-CV-4115, Docket Entry No. 113 ("Pfs.' SJ Fact Proffer"). These notes indicate that physicians who prescribed Zyprexa to UFCW Fund's insureds may have been falsely led into believing that Zyprexa was effective for a variety of problems for which it was not useful, including depression, mood disorders, anxiety, sleep problems, selective serotonin reuptake inhibitors ("SSRIs") failures, and dementia. *Id.*

b. Mid-West

Plaintiff Mid-West National Life Insurance Company of Tennessee ("Mid-West") is an insurance company based in North Richland Hills, Texas. Mid-West offers various insurance products, some of which include a prescription drug benefit. Dep. Tr. of Kip Howard on behalf of Plaintiff Mid-West at 100:8-20, Oct. 24, 2006 ("Mid-West Dep."). The numbers of persons covered by Mid-West for pharmacy benefits for the years 1999 through 2006 are as follows: 2,356 in 1999, 1,313 in 2000, 36,244 in 2001, 138,472 in 2002, 182,847 in 2003, 197,950 in 2004, 204,096 in 2005, and 223,069 in 2006. *See* Affidavit of Kip Howard at ¶ 3, Dec. 29, 2006 ("Mid-West Aff. 1"). No information is available on the number of persons covered for the years 1996, 1997, and 1998.

Mid-West's Plan A has a $50 deductible and a maximum annual coverage of $500. *Id.* Under Plan A, the insured receives a 25% discount on payments for brand-name drugs at the point of sale; the co-pay for generic drugs is a flat rate of $20 or $10 depending on how the prescription is filled. *Id.* Plan B has a deductible of $100 and a maximum annual coverage of $1000. Under Plan B, both generic and brand drugs are covered under a tiered flat co-pay of $15, $30, or $45, depending on whether the drug is generic, brand on-formulary, or brand off-formulary. *Id.*

Wholly owned by HealthMarkets, Inc. ("HealthMarkets"), Mid-West Aff. 1 at ¶ 2, Midwest has assets in excess of $25,000. Affidavit of Mid-West, Kip Howard, Jan. 5, 2007 ("Mid-West Aff. 2") at ¶ 2; Mid-West Dep. 13. From 1996 to present, either HealthMarkets or another company it wholly owns, MEGA Life and Health Insurance ("MEGA"), has contracted with a PBM to administer pharmacy benefits for Mid-West's insureds. Mid-West Aff. 1 at ¶ 2. Pharmacy benefits are administered by the PBM pursuant to contracts between HealthMarkets (or MEGA) and the PBM. *Id.*

The PBM that administered pharmacy benefits for Mid-West's insureds from 1996 through 1999 was Advanced Paradigm, Inc. (n/k/a Caremark, Rx, Inc.). Mid-West's Obj. & Answers to Lilly's First Set of Interrogs. ("Mid-West's Resps. to Interrogs., First Set") at No. 1. From 2000 through 2002, Mid-West's PBM was MedCo Health Solutions, Inc. *See id.* From 2003 through the present, Mid-West's PBM has been Caremark Rx, Inc. *See id.*

Mid-West always adopts the formulary of its PBMs; it does not create its own custom formulary. Mid-West Aff. 2 at ¶ 7. The formulary is set and controlled by its PBM. *Id.* Mid-West does cover non-formulary drugs, but its insureds pay a higher co-pay for them. *Id.* at ¶ 5. Zyprexa has always been on the formulary of Mid-West's PBM. *Id.* at ¶ 3.

Insureds of Mid-West with a prescription drug benefit are reimbursed, and have always been reimbursed, for eligible Zyprexa prescriptions. *Id.* at ¶ 4. Mid-West has never sought any utilization restrictions (including prior authorizations) for Zyprexa. *Id.* at ¶ 8. Since filing its complaint, it has not altered its practices or policies regarding its payment for Zyprexa. Mid-West Dep. 87-88; Mid-West's Resps. to Interrogs., First Set at No. 7. Mid-West pays a higher

price for Zyprexa now than when the Amended Complaint was filed; Zyprexa's market price has steadily increased at more than the cost-of-living.

Mid-West alleges that it has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. Am. Compl. at ¶¶ 472, 480, 535, 54, 546. It asserts that every Zyprexa prescription for which it has paid was procured by Lilly's alleged fraud. Opp'n to Mot. to Compel at 7. It has produced its prescription claim data in discovery, including information such as cost, dose, date, and identity of some prescribing physicians.

From January 2000 through April 2007, Mid-West paid for 1,617 Zyprexa prescriptions for 646 of its insureds. *See* Mid-West's Resps. to Interrogs., First Set, as supplemented. Mid-West does not possess claims data prior to January 2000. *Id.* Its documented payments for Zyprexa total $32,570. *See id.*

The plaintiff has communicated neither with its insureds nor their physicians about the safety or efficacy of Zyprexa. It has not shared the allegations of this lawsuit with them.

c. Local 28

Local 28, a New York Taft-Hartley health and welfare fund, provides a prescription drug benefit to active and retired member of the Local 28 Sheet Metal Workers Union. It provides coverage for members living in the five boroughs of New York City as well as in Nassau and Suffolk counties. Dep. of John McGrath on behalf of Plaintiff Local 28 at 13, Nov. 10, 2006 ("Local 28 Dep."). It has 2,800 working members, 400 apprentices, and 1,800 retirees, all of whom are eligible for health benefits for themselves and their families. *Id.* In total, Local 28's

Workers Fund provides benefits for approximately 10,000 people, *id.* at 43, 134, including eligible members in twenty-nine states. *Id.* at 13.

The pharmacy benefit plan for Local 28 is an "open plan;" payment is made for any drug as long as it is prescribed by a physician and is approved and non-experimental. *Id.* at 48-49. Since 2004, Local 28's formulary has been provided by its PBM, Specialized Pharmacy Solutions. The PBM has the exclusive authority to classify drugs in the formulary. *Id.* at 61-62. Local 28 pays any remaining balance for a prescription after a member provides the co-pay. *See also id.* at 84. It pays for Zyprexa and has not made any Zyprexa-specific changes to its policies. *Id.* at 33.

Alleged is that Local 28 has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. Am. Compl. at ¶¶ 472, 480, 535, 54, 546. It claims that every Zyprexa prescription for which it had paid was procured by Lilly's fraudulent conduct. Opp'n to Mot. to Compel 7. Local 28 has identified these prescriptions by producing claims data in discovery, including such information as cost, dose and date. Between 1998 and 2007, the Fund paid $198,906.73 for 848 Zyprexa prescriptions. Local 28 Dep. at Ex. 3.

Plaintiffs assert that certain call notes produced by Lilly indicates that Local 28's physicians were told that Zyprexa was effective for a variety of problems, including mood disorders, anxiety, sleep problems, SSRI failures and dementia; defendant disputes this interpretation. Lilly Physician Call Notes at ZY 1005511869, ZY 1005569827, ZY 1005599586.

d. SBA

The Sergeants Benevolent Association ("SBA") provides a prescription drug benefit, as well as other health benefits to sergeants in the New York City Police Department, retirees, and dependants. Dep. of Errol Ogman on behalf of Plaintiff SBA Health & Welfare Fund, Jan. 24, 2007 at 9:17-20 ("SBA Dep."). It provides pharmaceutical benefits for approximately 33,000 individuals. *Id.* at 9:17-20, 11:9-19, 145:10-15.

SBA pays for prescriptions, including those for Zyprexa, of covered members. *Id.* at 105:10-106:13. It has never used a formulary and does not distinguish between preferred and non-preferred drugs. *Id.* at 151-52. SBA has never imposed any restrictions (including prior authorizations, step therapy, or higher co-pays) for Zyprexa, *id.* at 150-51, 157, 159, although it has required prior authorization for other medications, including those used to treat schizophrenia. *Id.* at 212-14. SBA continues to pay for Zyprexa to this day. *Id.* at 36-37.

Third-party administrators handle SBA's routine benefit management. Until October 2003, SBA used General Prescription Program as its PBM. *Id.* at 162:24-163:10. In October 2003, SBA switched to a PBM named Caremark. *Id.*; SBA's Response to Interrogs. Caremark was the PBM for SBA from October 1, 2003 to July 31, 2005. SBA's Objs. & Answers to Lilly's First Set of Interrogatories, Jan. 17, 2007. In July 2005, SBA started a non-profit company called True Health Benefits to handle pharmacy benefit management. True Health Benefits then contracted with Innoviant Rx as a third-party administrator to handle the tasks of a normal pharmacy benefit manager. SBA Dep. at 50:8-20. SBA, acting through True Health Benefits, encourages participants to consider cost-effectiveness by requiring members to pay a percentage of the total drug cost rather than using a formulary. *Id.* at 147:6-148:4, 151:19-22.

SBA alleges that it has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. *Id.* at 33, 36-37. It asserts that every Zyprexa prescription for which it has paid was procured by Lilly's alleged fraud. *Id.* at 35-36. (From July 2001 to June 2005, SBA did not pay for Zyprexa medications for non-Medicare members because of a special New York City program that covered psychotropics for those patients. *Id.* at 152-55.) During the class period, SBA spent $87,869 for Zyprexa; it has identified these prescriptions by producing claims data in discovery.

Lilly allegedly made misleading statements to Caremark, SBA's PBM from October 2003 to July 2005. In May 2002, for instance, Caremark was contacted by a Lilly representative with information on a recent study finding that most atypicals were "significantly associated with diabetes mellitus" and that Zyprexa's metabolic effects were not worse than other SGAs', which plaintiffs claim downplayed Zyprexa's link to diabetes. *See* Letter from Vicki Poole Hoffman, Associate Therapeutic Consultant, Lilly U.S.A., Medical Division, to Audrey Moyna, Caremark, May 8, 2002; Ex. C to Def.'s Mem. Relating to the Form of Order on Class Cert. 2, Aug. 22, 2008, Docket No. 05-CV-4115, Docket Entry No. 222. Lilly also used Caremark and other PBMs to communicate and market to physicians. *See* Email from Paula J. McCain, Eli Lilly & Co., to Joanne Delois Murphy et al., Sept. 11, 2003, at 4:52:38 p.m. In September 2003, Lilly utilized Caremark to mail out Zyprexa marketing material to physicians. *Id.*

In June 2007, SBA notified its members about the pending litigation and concerns about Zyprexa. *See* SBA's Supp. Response to Interrogs., June 1, 2007. SBA continues to communicate with its members through its delegates regarding this litigation and concerns about Zyprexa. SBA Dep. at 121:18-122:17.

e. Teachers

Based in New York, plaintiff United Federation of Teachers Welfare Fund ("Teachers") provides supplemental health benefits to covered members, teachers, paraprofessionals, and eligible dependents. Teachers' Objections and Resps. to Lilly' First Set of Interrogs. at No. 1 (Teachers' Resps. to Interrogs., First Set"); Dep. Tr. of Arthur B. Pepper on behalf of Plaintiff Teachers at 7, Jan. 15, 2008 ("Teachers Dep."). Teachers offers various health products to its participants, including a prescription drug benefit.

An annual $100,000 maximum on prescription drug benefits is imposed per family per calendar year. UFT Welfare Fund Health and Welfare Benefits for Employees and Their Families 2007 Edition, 35, 50-51. The UFT Fund generally does not pay for medications for eligible persons in rest homes, nursing homes, sanitaria, extended-care facilities, and like entities unless pre-authorization is applied for and granted. *Id.* at 50.

It is Teachers' policy not to pay for any medications prescribed for off-label uses. Teachers' Resps. to Interrogs., First Set at No. 27; Teachers Dep. 42. It is the responsibility of Teacher's PBM to ensure that only prescriptions for covered medications are paid for by the UFT Fund. The UFT Fund relies on its PBM for such enforcement and monitoring.

Teachers reimburses eligible Zyprexa prescriptions for its covered members. Teachers' Resps. to Interrogs., First Set at No. 7. The formulary used by its PBM actually places Zyprexa in a preferred status. Teachers Dep. 71; 2007 Express Scripts National Preferred Formulary for UFT Welfare Fund. Like SBA, Teachers did not pay for any Zyprexa prescriptions from July 2001 until June 2005 for non-Medicare members because of the New York City program covering psychotropics. Teachers Dep. 79. Teachers continues to pay for Zyprexa.

Teachers alleges that it has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. It claims that every reimbursed Zyprexa prescription was procured by Lilly's fraudulent conduct and has identified these prescriptions by producing claims information about cost, dose, and date in discovery.

f. DC 37

Based in New York, plaintiff ASFCME District Council 37 Health and Security Fund ("DC 37") provides health benefits to member employees of the City of New York and their dependants. DC 37's Objections and Resps. to Lilly's First Set of Interrogs. at No. 1 ("DC 37's Resps. to Interrogs., First Set"); Dep. Tr. of Willie Chang on behalf of Plaintiff DC 37 at 24-25, Jan. 16 & Jan. 23, 2008 ("DC 37 Dep.").

DC 37 offers various health products to its participants, including a prescription drug benefit. Imposed is an annual $100,000 cap on prescription drug benefits. DC 37 Dep. 241. DC 37 does not pay for medicines administered to patients in rest homes, hospitals or other in-patient facilities. *Id.* at 242-43.

Adopting its PBM's recommendations, DC 37 does not independently seek to impose restrictions on particular drugs or classes of drugs. *Id.* at 158, 237. It has required prior authorization for other medications, including those used to treat schizophrenia, upon the advice of its PBM. *Id.* at 158-59, 235-37. It is DC 37's policy not to pay for any medications prescribed for off-label uses. DC 37's Resps. to Interrogs., First Set at No. 37; DC 27 Dep. 97, 147.

For covered participants, DC 37 reimburses eligible Zyprexa prescriptions. DC 37's Resps. to Interrogs., First Set at No. 1. From July 2001 until June 2005, DC 37 did not pay for psychotropics for its non-Medicare members because the City of New York program covered

those during that time, although it did cover Zyprexa prescriptions for Medicare-eligible retirees during that period. *Id.* DC 37 has not imposed or sought any restrictions (including prior authorizations, step therapy, or higher co-pays) or modifications to its formulary for Zyprexa. DC 37 Dep. 157-59, 237-38. It continues to pay for Zyprexa. *Id.* at 177.

DC 37 alleges that it has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. The Fund claims that every Zyprexa prescription for which it has reimbursed was procured by Lilly's alleged fraudulent conduct. It has identified these prescriptions by producing claims data in discovery, including information such as cost, dose and date.

2. Individual Plaintiffs

a. Michael Pronto

Plaintiff Michael Pronto, age 31, is a resident of Brentwood, New York. In April 2003, he became "sad and depressed" after a romantic setback. He sought counseling, and was referred to a nurse practitioner, Florence Wissert. Dep. Tr. of Florence Wissert at 27:3-9, Mar. 12, 2007 ("Wissert Dep.").

i. Use of Zyprexa

Pronto was first prescribed Zyprexa on April 28, 2003 through Nurse Wissert. *See* Pronto Dep. Ex. 4 at 5. He continued to receive prescriptions for Zyprexa from April 2003 through August 2003 and from April 2004 through the fall of 2006, at which time he stopped taking the medication. Dep. Tr. of Scott Sussman, N.P. at 79:24-80:15, April 23, 2007 ("Sussman Dep.").

Whether Pronto has bipolar disease is disputed. Nurse Wissert had no independent recollection of Pronto and her testimony was based solely on notes in his chart. Wissert Dep. 93:18-22. Medical records indicate that she used a screening tool, Lilly's one-page "Mood Disorder Questionnaire" ("MDQ"), to find that Pronto had bipolar disease, *id.* at 29:20-30:9, but the MDQ is not intended as a diagnostic tool. *See* Part XVIII.B.1.a, *infra*. Nurse Wissert also noted he had a history of alcohol abuse. Plaintiffs note that there is no evidence she performed a differential diagnosis, *see* Pronto Dep. Ex. 4 at 10, or used the criteria of the American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed., Washington DC, American Psychiatric Press Inc., 2000 ("DSM-IV-TR"). Neither did she utilize the Young Mania Rating Scale, which Lilly uses to evaluate patient improvement and efficacy of Zyprexa in treating Bipolar I., or the Axis V GAF. Sussman Dep. 79:24-80:15. *See generally* Pronto Dep. Ex. 4; Sussman Dep. Ex. 4.

Pronto was not treated by Nurse Wissert after August 8, 2003. Pronto Dep. Ex. 4 at 9. He did not receive medical care from anyone between that date and March 31, 2004, during which time it appears that he did not take Zyprexa. *Id.* Beginning March 31, 2004, Pronto was seen at the office of Dr. James Carlson. Sussman Dep. 38:11-21. Although Pronto received some care from Dr. Carlson, he was primarily seen by Scott Sussman ("Sussman"), a nurse practitioner. *Id.* From April 26, 2004 through October 23, 2006, Pronto was prescribed Zyprexa through Dr. Carlson's office. *Id.* at 50; Pronto Med. Rec. 6, 14-15.

When Nurse Sussman began treating Pronto on March 31, 2004, he prescribed Prozac for what he diagnosed as insomnia, depression, and anxiety. Pronto Dep. Ex. 5A at 1. At Pronto's next visit, on April 26, 2004, Sussman continued Prozac and added Ambien for insomnia.

Pronto Dep. Ex. 5 at 1. Nurse Sussman twice noted bipolar in Pronto's chart as a possible condition, but never attempted to determine whether Pronto actually had bipolar disorder. Sussman advised Pronto to see a psychiatrist, Sussman Dep. 52-53, 55, but he could not afford to do so. Dep. Tr. of Michael Pronto at 127:2-128:2, March 2-3, 2007 ("Pronto Dep.").

Pronto's diagnoses changed over the course of his treatment with Nurse Sussman and Dr. Carlson. Pronto Dep. Ex. 5 at 1. From December 17, 2004 onward, the focus of his treatment was a back and neck injury and its associated pain, Sussman Dep. 129:24-130:16, although Sussman noted Pronto's anxiety and panic disorder in his medical records that day. *See* Sussman Dep. Ex. 4.

In March 2006, Pronto advised Nurse Sussman that he had become aware of the Zyprexa litigation and wanted to have his blood sugar tested. Sussman Dep. 70-72. On September 25, 2006, he told a staff member in Dr. Carlson's office that he had been off Zyprexa for three months but wanted to resume treatment. *Id.* at 71-73, 146-47. On October 13, 2006, Pronto applied to Lilly's prescription drug program for free Zyprexa and received several months' supply. Pronto Dep. 149-52; Pronto Med. Rec. 12-13. It is unclear when Pronto actually last ingested Zyprexa.

ii. Payment for Zyprexa

During most of the relevant period, Pronto was insured through UFCW Local 1500, which provided a pharmacy benefit. The cost of his Zyprexa prescriptions was largely covered by insurance, except for a flat $25 co-payment per prescription. Pronto Dep. 49, 54. The total amount Pronto spent on Zyprexa is approximately $500.00. *Id.* at 19. When he lost his

insurance in June 2006, he was able to obtain Zyprexa free from his health care providers or directly from Lilly. *Id.* at 51-52, 56, 149-52; Pronto Med. Rec. 12-13.

iii. Effects of Zyprexa

Pronto claims he developed hypertension and high cholesterol and triglycerides as a result of Zyprexa. When he began the medication on April 28, 2003, Pronto weighed approximately 200 pounds. Wissert Dep. 33:22-34:7. In the first two or three months, he reportedly experienced a rapid weight gain of approximately forty to sixty pounds, Pronto Dep. 14:4-20, 62:6-63:1, complaining about it at his September 13, 2004 visit with Nurse Sussman. Sussman Dep. Ex. 4. After discontinuing Zyprexa in the fall of 2006, his weight dropped to 226 pounds by March 2, 2007. Pronto Dep. 14:19-20.

Pronto's baseline laboratory values were not recorded when he started taking Zyprexa. In April 2004, his blood pressure was moderately hypertensive. A month later, blood glucose levels, cholesterol, LDL, and triglycerides were all normal. In January 2005, Nurse Sussman diagnosed him as having hypertensive heart disease, unspecified. By April 2006, Pronto's glucose level was elevated and his triglyceride levels, LDL, and cholesterol were very high. *See* Pronto Med. Rec.

Lilly contends that the evidence shows that Zyprexa was effective for Pronto, highlighting his positive self-reporting noted in his medical charts. *See id.* at 1-3, 7, 8; Wissert Dep. at 51-52, 63; Sussman Dep. 65. Nurse Sussman continued to prescribe Zyprexa in April 2006 because "it was working for" Pronto. Sussman Dep. 76.

Plaintiffs allege, in contrast, that there is no evidence that Zyprexa was ever effective for Pronto. While Pronto did report he was "feeling better with his current medication," plaintiffs

note that such self-reporting is often unreliable; moreover, it is difficult to determine what medication he was on at the time of these comments and whether he was referring to his pain medication. *Id.* at 131:7-13.

While this individual's case is thin, there is enough to go to a jury. The claim of overpayment, based upon the evidence that the price charged was too high, could be accepted by a reasonable juror.

iv. Related Cases

To seek redress for his alleged physical injuries, Pronto has sued Lilly in a separate action. That case is in the process of settlement. *See Pronto v. Eli Lilly & Co.*, Docket No. 06-CV-6834 (E.D.N.Y.) (administratively closed, pending final consummation of settlement). The general releases being used in these personal injury cases prevent a case such as the instant one from being brought by this plaintiff.

In an affirmation filed on June 23, 2008, Pronto's counsel states that the plaintiff has not

> settled any of his claims against Lilly and [has not] executed any release whatsoever of any claims against Lilly. Moreover, as described below, during discovery, defendant Eli Lilly and Company ("Lilly") agreed to treat Mr. Vannello's claims for economic injury, based on his purchases of Zyprexa, separately from his claims for physical injury based on his ingestion of Zyprexa. Based on this separation of the two types of claims, it is my understanding that, even if Mr. [Pronto] were to settle his physical injury claims, he would not release, and would not be asked to release, his purchase claims.

Aff. of Douglas R. Plymale 3, June 23, 2008, Docket No. 05-CV-4115, Docket Entry No. 197.

This portion of plaintiff's counsel's statement is contradicted by Lilly's response of June 23, 2008; Lilly indicates that Pronto is in the process of settling his case as part of a global settlement, with a "Master Settlement Agreement on behalf of . . . Zyprexa clients, including

plaintiffs" Michael Pronto and Michael Vannello. Def.'s Br., June 23, 2008, at 2 (filed under seal). Their cases were administratively closed by order of the court on March 18, 2008, with no objection or motion to set aside or modify the order. *Id.*

The release required by the Master Settlement Agreement covering the Pronto and Vannello claims is broad enough to cover overcharge claims for Zyprexa. It reads:

> Claimant KNOWINGLY AND VOLUNTARILY RELEASES, ACQUITS, AND FOREVER DISCHARGES Lilly from any and all claims and/or causes of action of whatever kind or character, which have accrued or may accrue, whether known or unknown, and includes, but is not limited to, those claims which Claimant ever had, or now has, or hereafter can, shall or may have in the future against Lilly arising out of, relating to, resulting from, or in any way connected with Zyprexa, including those claims and damages of which Claimant is not aware and/or that Claimant has not yet anticipated. Claimant expressly waives the provisions of any applicable law protecting against the release of unknown or unanticipated claims.

Id. at 3. It is probable that the settlement will ultimately be fully executed, making the release operative; it would likely result in dismissal of plaintiffs' individual economic claims based on the general exhaustive terms of the release.

If the tentative global agreement already reached falls through, there is a conflict of interest. Plaintiff may "sell out" the proposed economic class to achieve a higher award in his personal injury claim. He cannot represent a class or subclass seeking compensation for overpayment without appearing to violate fiduciary responsibilities to the class.

In any event, the individual plaintiffs who are settling, or have settled, their personal injury claims would have to be excluded from the class, as plaintiffs' counsel practically concedes:

> Because at least some plaintiffs who have settled personal injury claims may have released their over-payment claims, however, Plaintiffs provide an adjusted definition for the Consumer Class to reflect the exclusion from the class of individuals who

> have released their claims. Plaintiffs had previously acknowledged that such persons would be excluded from the class; the adjusted definition merely formalizes that position and incorporates it into the class definition for ease of application.

Pfs.'s Submission Regarding Consumer Class Members' Releases 2, June 23, 2008, Docket No. 05-CV-4115, Docket Entry No. 196. Such a possible large carve-out of some 30,000 plaintiffs would unduly complicate administration of the litigation.

It may be that some of the third-party payors in the class will seek reimbursement from their insureds based on the personal injury recoveries. This possibility is of such minor significance as to warrant its being ignored at this stage of the litigation.

b. Michael Vannello

Plaintiff Michael Vannello, aged 54, is a resident of Ridgewood, Queens, New York. In 1995, he developed panic attacks and fear associated with riding the subway in New York City. He left his longstanding messenger job at First Manhattan Company, Dep. Tr. of Michael Vannello at 36:6-23, 80:25-81:9, Mar. 1, 2007 ("Vannello Dep."), and applied for and was granted Social Security Disability Insurance. *See* Dep. Tr. of Ronald Vannello, April 30, 2007 ("Ron Vannello Dep.") at 23:23-24:5. His brother, Ronald Vannello, is his representative payee for his monthly disability payments. *Id.* at 8:23-9:9.

i. Use of Zyprexa

Vannello was treated with multiple medications during the 1990s, including antidepressants and anti-anxiety medication. He was initially prescribed Zyprexa by his treating psychiatrist in February 2000, and took Zyprexa almost continuously to October 2002. He did not take Zyprexa for schizophrenia or bipolar disorder.

In March 1995, Laszlo Papp, M.D., a psychiatrist and professor at Columbia University, diagnosed Vannello as having panic disorder and anxiety disorder. Dep. Tr. of Dr. Lazlo Papp, Apr. 24, 2007 ("Papp Dep.") at 11, 14, 16. Dr. Papp first prescribed Zyprexa on February 22, 2000 at a 5 mg level, after Vannello had complained that he was nervous and worried with mood swings and angry outbursts, and had trouble sleeping. *Id.* at 86; Select Medical Records of Michael Vannello 16-17 ("Vannello Med. Rec.").

In March 2000, Dr. Papp referred Vannello to an intensive outpatient treatment program at Zucker Hillside Hospital, where he continued to be prescribed Zyprexa. *Id.* at 22-30. All of Vannello's Zyprexa prescriptions were for off-label uses while he was being treated at Hillside. *See* Dep. Tr. of Dr. Michael Kahan at 146:18-147:20, Apr. 11, 2007 ("Kahan Dep."). On June 30, 2000, Dr. Michael Kahan, a psychiatrist and head of the hospital's outpatient anxiety disorder program, diagnosed Vannello with a panic disorder with agoraphobia and continued him on Zyprexa at 5 mg daily, along with Xanax 1 mg four times a day.

While at Hillside, Vannello attended group therapy, received individual counseling from a clinical social worker, and was prescribed medication. Kahan Dep. Ex. 2. He received a variety of medications in addition to Zyprexa. *Id.* Dr. Kahan discontinued Vannello's Zyprexa use for three months starting in January 2001, but in March he began it again at an increased dosage of 7.5 mg. On June 29, 2001, Dr. Kahan further increased the dosage to 10 mg, raising it to 15 mg on August 14, 2001. On September 19, 2001, Dr. Kahan again increased the dosage to 20 mg because Vannello's anxiety had been increasing. *Id.* at 41-42. Vannello took Zyprexa for general anxiety disorder and panic disorder with agoraphobia until September 27, 2002. Ron Vannello Dep. at 69; Vannello Med. Rec. 39-40, 53; Kahan Dep. 30-31, 44, 108.

ii. Payment for Zyprexa

Vannello paid approximately $5,932.00 in cash for his Zyprexa prescriptions. *See* Mem. Supp. of Pfs.' Mot. for Class Cert. 54; Michael Vannello Eckerd Drug Prescription Records. He also received free samples of Zyprexa from his doctors. Kahan Dep. 106; Vannello Dep. 55.

iii. Effects of Zyprexa

Before he began taking Zyprexa in 2000, Vannello had a history of obesity and diabetes. Since 1993, his doctors have recommended a weight reduction diet. Vannello Med. Rec. 5, 7-8. Vannello was first treated for hypertension in March 1991, *id.* at 1, for adult onset diabetes mellitus on March 21, 1995, Dep. Tr. of Dr. Lewis Bass, M.D., May 14, 2007 ("Bass Dep.") at 68-69, and for high cholesterol in November 1996. Vannello Med. Rec. at 19.

At the time of his initial diabetes diagnosis in 1995, Mr. Vannello weighed 293 pounds. *See* Kahan Dep. Ex. 10 at 57. He was able to control his weight and diabetes without medication, Bass Dep. 68:23-69:9, losing 90 pounds over the next two years. *See* Kahan Dep. Ex. 10 at 45. After Vannello's weight dropped, he had no symptoms of diabetes. *See id.* at 45.

When Vannello began to take Zyprexa in February 2000, he weighed 240 pounds, *see* Papp. Dep. Ex. 3 at 5, and he was not taking any diabetes medications. Bass Dep. 68:23-69:9. By March 21, 2000, Vannello had gained 16 pounds. *See* Papp. Dep. Ex. 3 at 6. Over the next two years while on Zyprexa, his weight increased dramatically, reaching 314 pounds by August 2002. *See* Kahan Dep. Ex. 10 at 36. Vannello's Zyprexa treatment was discontinued in October 2002, around the time he reached his peak weight. Bass Dep. Ex. 3.

Vannello was again diagnosed with diabetes mellitus in May 2003. Bass Dep. 54. His fasting blood glucose levels peaked at 388 mg/dl around this time. *See* Kahan Dep. Ex. 10 at 32.

Similarly, Vannello's triglycerides were measured at 404 in early 2004; he had no previous record of triglycerides or total cholesterol elevation prior to this time. It took almost three years to drop to his pre-Zyprexa weight of 242 pounds. *Id.* He currently takes Metformin to treat his diabetes. Vannello Dep. 10, 167.

Vannello underwent a number of echocardiograms before, during, and after his Zyprexa treatment. A pre-Zyprexa echocardiogram on November 9, 1999, showed evidence of left atrial dilation and left ventricular hypertrophy. *See* Bass Dep. Ex. 3. A post-Zyprexa echocardiogram on May 12, 2001 revealed a dilated left ventricle in addition to left atrial dilation and left ventricular hypertrophy. Bass Dep. Ex. 4. EKGs in December 3, 2002, *see* Bass Dep. 43, and 2006 suggested continuing ischemic heart disease. Bass Dep. Ex. 6. Vannello's obesity, combined with pre-existing hypertension, may have caused excess strain on the heart muscle, possibly resulting in permanent damage. Bass Dep. 100:23-102:3; Decl. of William Wirshing, M.D. 6-7, 16, 48-49, Jan. 31, 2007 ("Wirshing Decl."); Expert Witness Rep. & Decl. of David Allison, Ph.D. 10; 23-24, Feb. 12, 2007 ("Allison Rep.").

Lilly maintains that the evidence shows that Zyprexa was effective for Mr. Vannello, citing positive self-reports noted in his medical charts, such as feeling less irritable, under better control, less anxious, improved mood, and getting out more. Vannello Med. Rec. 17, 31-33, 37-38, 56; Vannello Dep. 99-100; Papp Dep. 47-48. Vannello's symptoms worsened when Dr. Kahan tried to take him off Zyprexa in January 2001, and he reported feeling better after restarting Zyprexa in March 2001. Kahan Dep. 31-32.

Plaintiffs note there is no objective medical evidence—as opposed to Vannello's own self-reports—to indicate that Zyprexa was efficacious in treating him. *See* Fed. R. Evid. 702.

During the course of his treatment at Hillside, his diagnoses remained consistent. *See* Kahan Dep. Ex. 2. At the time of Vannello's discharge in November 2002, his diagnoses were still panic disorder with agoraphobia and general anxiety disorder. *Id.* at 210-12. None of the treating doctors prescribing Zyprexa used the Young Mania Ratings Scale ("Y-MRS"). On Axis V of the DSM-IV-TR, another standard measure of mental/emotional function, Vannello showed no improvement; his Global Assessment of Functioning Scale ("GAF") was 50/60 when he was admitted on March 20, 2000 to Hillside Hospital. *Id.*

iv. Related Cases

Vannello has filed a separate personal injury action against Lilly claiming a diabetes injury as a result of Zyprexa ingestion. *See Vannello v. Eli Lilly & Co.*, Docket No. 06-CV-6839 (E.D.N.Y.) (administratively closed, pending final consummation of settlement). For the same reason as in Mr. Pronto's case, *see* Part II.A.2.a.iv, *supra*, Mr. Vannello cannot represent the proposed class or subclass.

B. Prior Submissions

Multiple prior submissions define the claims, evidence, and facts of the dispute. Except for the plaintiffs' original individual complaints, all submissions are docketed under Docket No. 05-CV-4115 (E.D.N.Y.). *See* First Am. Class Action Compl. & Demand for Jury Trial, Nov. 7, 2005, Docket Entry No. 14 (redacted); Def.'s Answer, Apr. 26, 2007, Docket Entry No. 107; Def.'s Mot. to Dismiss First Am. Compl., Jan. 12, 2006, Docket Entry No. 22; Pfs.' Mem. of Law in Opp. to Def.'s Mot. to Dismiss, Feb. 23, 2006, Docket Entry No. 27; Def.'s Reply Mem. of Law in Further Support of Mot. to Dismiss, Mar. 24, 2006, Docket Entry No. 31; Def.'s Mot. for Summary J., May 29, 2007, Docket Entry No. 109; Pfs.' Mem. of Law in Opp'n to Def.'s

Mot. for Summary J., June 12, 2007, Docket Entry No. 113; Def.'s Reply Mem. in Support of Def.'s Mot. for Summary J., June 18, 2007, Docket Entry No. 121; Def.'s Local R. 56.1 Statement of Undisputed Facts, May 29, 2007, Docket Entry No. 109; Pfs.' SJ Fact Proffer; Pfs.' Submission Regarding Consumer Class Members' Releases, June 23, 2008, Docket Entry No. 196; Def.'s Response Regarding Information on Settlement of Sub-Class Representatives' Claims, June 23, 2008, Docket Entry No. 198 (sealed); Pfs.' Reply Submission Regarding Consumer Class Members' Releases, June 25, 2008, Docket Entry No. 199; Def.'s Mem. Relating to the Form of an Order on Class Cert., Section 1292(b) Cert., Aug. 22, 2008, Docket Entry Nos. 228, 230.

C. Unsealing Motions

From its inception over four years ago, this litigation has been subject to a protective sealing order pursuant to Rule 26 of the Federal Rules of Civil Procedure, applying to the products of discovery and all derived documents. Case Mgmt. Order No. 3, Aug. 3, 2004, Docket No. 04-MD-1596, Docket Entry No. 61 (limited to cases alleging personal injury from ingestion of Zyprexa); *see* Fed. R. Civ. P. 26(c). An identical protective order specifically applicable to the third-party payors cases was issued on October 16, 2006, Case Mgmt. Order No. 3, Oct. 16, 2006, Docket No. 05-CV-4115, Docket Entry. No. 61, and a second one applicable to financial data a month later. Case Mgmt. Order No. 4, Nov. 17, 2006, Docket Entry. No. 72. Since the inception of the case, millions of documents produced by Lilly have been marked confidential.

Along with their first amended complaint, filed November 7, 2005, plaintiffs moved to declassify certain Lilly documents cited in the complaint. Notice of Pfs.' Action to Lift

Confidentiality Designations, Nov. 7, 2005, Docket Entry No. 15. Plaintiffs argued that Lilly's "documents cited in the First Amended Complaint do not 'contain trade secrets or other confidential research, development, or commercial information' or other material properly protected under Federal Rule of Civil Procedure 26(c)(7), and that the documents are improperly designated as 'confidential' under the protective order." *Id.* Both parties briefed the issue for decision by the special master supervising discovery. *See* Lilly Letter, Apr. 19, 2006, Docket Entry No. 37.

In January 2007, plaintiffs renewed their declassification motion, which had not yet been resolved. The motion was deferred, *see* Order, Feb. 7, 2007, Docket Entry No. 85, pending resolution of the injunction proceedings related to the *New York Times*' December 2006 publication of a series of articles revealing confidential information obtained illegally from the Zyprexa MDL. *See In re Zyprexa Injunction*, 474 F. Supp. 2d 385 (E.D.N.Y. 2007). Plaintiffs also challenged the confidentiality designations of all of defendant's documents cited in defendant's experts' reports, for the same reasons as in their previous motion. *See* Notice of Pfs.' Action to Lift Confidentiality Designations, Mar. 9, 2007, Docket Entry No. 91; *see* Pfs.' Letter, Mar. 23, 2007, Docket Entry No. 93 (requesting a hearing). The motion was referred to the special master to review the documents and determine which should be unsealed. Order, Mar. 30, 2007, Docket Entry No. 104.

On July 7, 2007, plaintiffs challenged the confidentiality designations of all the documents produced by defendant that were cited in plaintiffs' summary judgment and *Daubert* pleadings. Notice of Pfs.' Action to Lift Confidentiality Designations, July 7, 2007, Docket Entry No. 130. On April 2, 2008, plaintiffs wrote to the court requesting that the declassification

process by the special master be completed. As of that date, plaintiffs challenged the confidentiality of 351 documents produced by Lilly, as well as the marketing and sales data covered by Case Management Order No. 4. Pfs.' Letter, Apr. 2, 2008, Docket Entry No. 172.

Plaintiffs then moved under Rule 23(d) of the Federal Rules of Civil Procedure for an order permitting the publication of documents on the basis of which the parties made their dispositive motions, including class certification. *See* Pfs.' Notice of Mot. & Mem. in Support, Aug. 4, 2008, Docket No. 05-CV-4115, Docket Entry Nos. 215-16; Pfs.' Reply, Aug. 22, 2008, Docket Entry No. 225; Fed. R. Civ. P. 23(d)(1)(B)(iii) ("In conducting an action under this rule, the court may issue orders that: . . . require—to protect class members and fairly conduct the action—giving appropriate notice to some or all class members . . . (iii) the members' opportunity to signify whether they consider the representation fair and adequate, to intervene and present claims or defenses, or to otherwise come into the action."). Several non-parties also requested that the documents be unsealed. *See* Letter, Bloomberg L.P., Aug. 18, 2008, Docket No. 04-MD-1596, Docket Entry No. 1832; Mot. to Vacate CMO 3, Vera Sharav, Alliance for Human Research Protection & David Cohen, Docket No. 04-MD-1596, Docket Entry No. 1859; Letter, Kaiser Health Foundation Plan et al., Aug. 22, 2008, Docket No. 04-MD-1596, Docket Entry No. 1847. Defendant opposed, citing trade secrets and arguing the documents contain commercially valuable information. Def.'s Mot. in Opp'n, Aug. 18, 2008, Docket Entry No. 222. This motion was argued at a hearing on September 4, 2008.

Based on this country's long-standing tradition of open access to the courts and court records, the enormous number of people who have taken or will take Zyprexa, the involvement

of government regulatory bodies, absent class members' interest in the proceeding, and the age of the documents, the motions to unseal are granted. *See* Part XXIV, *infra.*

D. Dispositive Motions

1. Motion to Dismiss

On January 12, 2006, Lilly filed a Rule 12 motion to dismiss plaintiffs' Amended Complaint on the grounds that plaintiffs could not satisfy the causation element of their claims, that they lack standing, and that they suffered no direct injury. Def.'s Mot. to Dismiss First Am. Compl.; Def.'s Reply Mem. of Law in Further Support of Mot. to Dismiss. In response, plaintiffs assured the court that they would offer evidence that would demonstrate causation and reliance, Apr. 21, 2006 Hr'g Tr. on Def.'s Mot. to Dismiss 27, Docket Entry No. 36, and alleged as follows:

> [I]t will be proven as fact not presumption, that every influential sector of the mental health community was subjected to Defendant's misrepresentations and omissions, and that the broad-based fraudulent conduct had real-world, significant effect that was intended by the program.

Pfs.' Mem. of Law in Opp. to Def.'s Mot. to Dismiss 30.

Lilly's Motion to Dismiss was denied on April 21, 2006. *See* Minute Entry, Apr. 21, 2006, Docket Entry No. 36.

2. Summary Judgment

Instead of a motion to dismiss, the court preferred to rule on a summary judgment motion. It directed the parties to work with the Special Master to establish a limited discovery plan. Apr. 21, 2006 Hr'g Tr. 43-49; *see* Am. Case Mgmt. Order No. 1, June 19, 2006, Docket Entry No. 39. Discovery was confined to the grounds for summary judgment. *Id.* at 3-6; Apr. 21, 2006 Hr'g Tr.

43-49. The discovery undertaken by both parties is discussed at length in Lilly's May 29, 2007 Memorandum of Law in Support of its Motion for Summary Judgment. Plaintiffs were given access to all of the discovery taken in the personal injury litigation, which comprised over fifteen million pages of records and included the depositions of fifty-eight current and former Lilly employees.

Lilly conducted Rule 30(b)(6) depositions of the four original named payor plaintiffs UFCW, Mid-West, Local 28, and SBA. Testimony was obtained from the four PBMs that provide pharmacy benefit advice to the named plaintiffs. Lilly also undertook discovery regarding the two individual plaintiffs, deposing them, their family members, and prescribers.

Both parties produced a number of expert witness reports and deposed the experts. Plaintiffs submitted expert reports by Meredith Rosenthal, Ph.D.; Jeffrey E. Harris, M.D., Ph.D.; John Abramson, M.D.; Steven G. Klotz, M.D.; Lon Schneider, M.D., and Robert Rosenheck, M.D. *See* Pfs.' Disclosure of Expert Testimony Pursuant to Fed. R. Civ. P. 26(a)(2), Feb. 27, 2007, Docket Entry No. 87 (designating plaintiffs' experts). Two plaintiffs' experts, Myron Winkelman, R.Ph., and Terry D. Leach, Pharm.D, proposed to testify about how PBMs function from economic and clinical perspectives. *Id.* Plaintiffs also relied on the following experts, previously disclosed in the personal injury litigation: David Goff, Jr., M.D.; David B. Allison, Ph.D.; Frederick Brancati, M.D., MHS; William Wirshing, M.D.; John L. Guerigian, M.D.; and Laura Plunkett, Ph.D., D.A.B.T. *Id.*; *see* Part XVIII, *infra*.

In support of its summary judgment motion, Lilly relied on five experts: Ernest R. Berndt, Ph.D.; Iain M. Cockburn, Ph.D.; David F. Feigal, Jr., M.D.; David Kahn, M.D.; and Jeffrey S. McCombs, Ph.D.

With a record developed by May of 2007, Lilly filed a motion for summary judgment on grounds similar to those in its motion to dismiss. Plaintiffs also filed a summary judgment motion. On June 28, 2007, the court denied both summary judgment motions and all of the various *Daubert* challenges to proposed expert testimony. *In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 579 (E.D.N.Y. 2007) ("While the case is close, plaintiffs have sufficiently demonstrated for purposes of this motion that genuine issues of material fact exist with respect to their RICO and state substantive law claims.").

Recognizing that the law underlying its decision was "in a state of flux and not free from doubt," the court declined to certify its summary judgment order for immediate interlocutory appeal pursuant to 28 U.S.C. § 1292(b), but noted that it would do so after deciding whether the case should proceed as a class action. *Id.* at 580-81.

E. Class Certification

On August 3, 2007, plaintiffs filed a motion for class certification. They proposed two subclasses: a nationwide third-party payor class of institutions that have paid for the cost of Zyprexa prescriptions, and a nationwide patient class of individuals who have paid out-of-pocket for some or all of the cost of Zyprexa prescriptions. Pfs.' Class Cert. Br. 58-59.

1. Briefing

Both parties filed extensive briefing. *See id.*; Class Plaintiffs' Proposed Trial and Apportionment Plan and Statement of State Law ("Pfs.' Trial Plan"), Dec. 4, 2007, Docket Entry No. 144; Defendant's Memorandum of Law in Opposition to Plaintiffs' Motion for Class Certification ("Def.'s Mem. of Law in Opp. to Class Cert."), Feb. 22, 2008, Docket Entry No. 150 (filed under seal); Defendant's Statement of Facts in Support of Defendant's Opposition to

Plaintiff's Motion for Class Certification ("Def.'s Fact Proffer"), Def.'s Local R. 56.1 Statement of Undisputed Facts, Feb. 22, 2008, Docket Entry No. 150; Plaintiffs' Reply Memorandum of Law in Further Support of Purchase Claim Plaintiffs' Motion for Class Certification (Pfs.' Reply Mem. of Law in Further Support of Purchase Claim Pfs.' Mot. for Class Cert.), Mar. 21, 2008; Plaintiffs' Response to Defendant's Local Rule 56.1 Statement of Undisputed Facts (Pfs.' Response to Def.'s Fact Proffer"), Mar. 21, 2008, Docket Entry No. 165; Plaintiffs' Post-Hearing Memorandum on Class Certification, ("Pfs.' Post-Hr'g Mem. on Class Cert."), Apr. 9, 2008, Docket Entry No. 176; Defendant's Post-Hearing Memorandum Opposing Class Certification, ("Def.'s Post-Hr'g Mem. Opp. Class Cert."), Apr. 9, 2008, Docket Entry No. 177.

2. Discovery

In filing their motion for class certification shortly after summary judgment was denied, plaintiffs indicated they did not believe additional discovery on class certification was necessary. *See* Pfs.' Class Cert. Br., Aug. 3, 2007. In response, Lilly moved for additional discovery on class certification. At a hearing on Lilly's motion on September 21, 2007, the court agreed that the record contained little evidence regarding differences in the ways that third-party payors in the putative class develop and maintain their formularies:

> What concerns me is the differences in the nature of these insurers and now how they went about doing their research, putting their formularies together, using experts, what their insurance plans called for in connection with reimbursement, whether they were reimbursing fully or whether there was also a requirement that the insured paid a portion.

Sept. 21, 2007 Hr'g Tr. 18-19. More information in these areas was necessary to determine whether the proposed class was sufficiently homogenous. *Id.* at 29.

On November 30, 2007, a conference was held to discuss the scope of additional class certification discovery, including the depositions of the named payors' insureds' prescribers. *See* Nov. 30, 2007 Hr'g Tr. While it was willing to permit the limited class certification discovery previously ordered by the special master to go forward as contemplated, *id.* at 35, the court also suggested that the information sought by the plaintiffs was not necessary for class certification. *Id.* at 23 ("I'm very skeptical about whether we need [additional call note and database production]"). Instead, the court recommended that the parties "just close [discovery] out at this stage and go forward with certification based on the enormous amount of papers and other material that we have in this case and in other cases." *Id.* at 35. The parties agreed; the only further discovery undertaken was Lilly's depositions of newly identified class representatives and one of UFCW's PBMs. *Id.* at 37-38. Depositions previously taken in this and other matters were to be used to present the class certification issue, although their admissibility could still be challenged at trial. *Id.* at 37. Case Management Order No. 9 reflected this agreement and was entered on December 21, 2007. *See* CMO 9, Nov. 21, 2007, Docket Entry No. 146.

3. Expert Reports

Preparing for an evidentiary hearing on class certification, both parties relied on the same experts presented to the court on the issue of summary judgment. *See* Part XVIII, *infra*. Defendants also presented a new expert, Dr. Eugene Kolassa. Additional expert reports were submitted on the issue of class certification.

All *Daubert* motions as to proposed expert witnesses, whether made as part of the class certification motion or in earlier proceedings, have been denied.

> Each of the challenged experts meets *Daubert* requirements. Each is a distinguished scientist whose expertise probably will be helpful in deciding relevant scientific and economic issues. Attacks on them . . . are primarily based on assessments of credibility best left for the trier. *In limine* motions respecting particular aspects of these and other experts' proposed testimony will be considered when it becomes clear what will be the detailed issues to be tried.

In re Zyprexa Prods. Liab. Litig., 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

Four days before the hearing, on March 24, 2008, Lilly filed a Motion to Strike as untimely and prejudicial the Supplemental Declaration of Robert Rosenheck, M.D., the Supplemental Declaration of William Wirshing, M.D. and the Second Supplemental Declaration of Meredith Rosenthal, Ph.D. *See* Def.'s Mot. to Strike, Mar. 24, 2008, Docket Entry Nos. 160, 161. At the March 29, 2008 hearing, defendant's motion was denied. *See* Transcript of Evidentiary Proceedings on Class Certification, March 28, 2008 through April 2, 2008 ("Tr."); *see also* Pfs.' Mot. to Strike Decl. of Alan G. White, Ph.D., June 12, 2007, Docket Entry Nos. 114, 115.

4. Evidentiary Hearing

On March 28-31 and April 1-2 of 2008 an extensive evidentiary hearing was conducted to comply with the certification standards set by the Court of Appeals for the Second Circuit. *See In re Initial Public Offering Securities Litigation* ("*In re IPO*"), 471 F.3d 24, 41 (2d Cir. 2006) (noting that even when there is overlap between a Rule 23 requirement and a merits issue, "the district judge must receive enough evidence, by affidavits, documents, or testimony, to be satisfied that each Rule 23 requirement has been met."). Extensive oral and written expert testimony was considered. More than 1,000 exhibits, the majority of which had been previously submitted, were admitted.

On April 2, 2008, the court granted leave to the parties to file post-hearing memoranda. *See* Pfs.' Post-Hr'g Mem. on Class Cert.; Def.'s Post-Hr'g Mem. Opp. Class Cert. Further argument was heard on April 10, 2008. Additional submissions were requested and received. *See* Pfs.' Corr. Supp. Post-Hr'g Mem. on Class Cert.; Affirm. of Andrea Bierstein in Support of Purchase Claim Pfs.' Supp. Post-Hr'g Mem. on Class Cert (undocketed); Affirm. of Thomas Sobol in Connection with Damages Calculations, Apr. 24, 2008, Docket Entry No. 180; Def.'s Supp. Post-Hr'g Mem. of Law, Apr. 24, 2008, Docket Entry No. 181. Supplemental authority letters were submitted. *See* Letter from Lauren G. Barnes, May 20, 2008, Docket Entry No. 189 (noting *New England Carpenters Health Benefits Fund v. First Databank, Inc.*, 248 F.R.D. 363 (D. Mass 2008); Lilly Letter, May 22, 2008, Docket Entry No. 190 (same); Pfs.' Notice of Supp. Authority, June 9, 2008, Docket Entry No. 191 (noting *Bridge v. Phoenix Bond & Indemnity Co.*, 128 S. Ct. 2131 (2008)); Def.'s Mem. in Opp. to Notice of Supp. Authority, June 10, 2008, Docket Entry No. 192; Pfs.' Reply in Support of Notice of Supp. Authority, June 11, 2008, Docket Entry No. 193.

Further information about the status of the two individual plaintiffs' personal injury lawsuits against Lilly and their proposed settlement releases was requested. *See* Purchase Claim Pfs.' Submission Regarding Consumer Class Members' Releases, June 23, 2008, Docket Entry No. 196; Def.'s Response Regarding Information on Settlement of Sub-Class Representatives' Claims, June 23, 2008, Docket Entry No. 198 (sealed); Pfs.' Reply Submission Regarding Consumer Class Members' Releases, June 25, 2008, Docket Entry No. 199; Pfs.' Reply Affirmation of Kevin L. Oufnac, June 25, 2008, Docket Entry No. 200; Affirmation of Dr. Douglas R. Plymale, June 19, 2008, Docket Entry No. 197.

Additional briefing was requested on the combined impact of the Second Circuit Court of Appeals decision in *McLaughlin v. American Tobacco Co.*, 522 F.3d 215 (2d Cir. 2008), and the Supreme Court's opinion in *Bridge v. Phoenix Bond & Indemnity Co.*, 128 S. Ct. 2131 (2008), on the pending motion for class certification. *See* Order, June 16, 2008, Docket Entry No. 195.

After the court's discussion draft on certification was issued on July 2, 2008, the parties were given an opportunity to further brief and argue certification-related issues. *See* Hr'g Tr., July 17, 2008; Oral Statement by the Court at Class Cert. Hr'g, July 17, 2008, Docket No. 05-CV-4115, Docket Entry No. 207; Order, July 17, 2008, Docket Entry No. 208; Order on Potential Conflict of Interests, July 21, 2008, Docket Entry No. 210; Pfs.' Mem. in Response to the July 21, 2008 Order Regarding *Amchem* Issues, Aug. 4, 2008, Docket Entry No. 214; Def.'s Response to the July 21, 2008 Order Regarding Potential Conflicts of Interest, Aug. 4, 2008, Docket Entry No. 211; Purchase Claim Pfs.' Mem. Final Supp. Submission Regarding Class Cert. and Cert. Under 28 U.S.C. § 1292, Aug. 22, 2008, Docket Entry No. 226; Joint Notice Program, Aug. 22, 2008, Docket Entry No. 227; Def.'s Mem. Relating to the Form of an Order on Class Cert., Section 1292(b), Aug. 22, 2008, Docket Entry Nos. 228, 230. A full opportunity was given to the parties and interested members of the public to comment on this court's draft certification order of July 2, 2008. *See* Part I.E, *supra*.

Each side has submitted a proposed certification order fulfilling the requirements of Rule 23(c), consistent with, and incorporating, the analysis and findings in the prior tentative proposed draft of this memorandum and order. *See* Pfs.' Proposed Order on Class Cert. attach. 1, Aug. 22, 2008, Docket Entry No. 227; Def.'s Proposed Order, Aug. 22, 2008, Docket Entry No.228 Ex. 1; *see* Fed. R. Civ. P. 23(c). Defendant notes that submission of the order does not constitute

agreement with any portion of this memorandum. The order is incorporated in the conclusion. *See* Part XXIV, *infra*.

Both parties have, assuming *arguendo* that the present memorandum and order will be approved by the Court of Appeals for the Second Circuit, agreed upon the notification procedures to be used under Rule 23(c)(2), including opt-out provisions and the like. *See* Joint Notice Program, Aug. 22, 2008, Docket Entry No. 227 attach. 2. The Notice Plan is attached in Appendix A, *infra*.

The expert reports and testimony considered by the court and contested by the parties in the instant motion are individually discussed in Part XVIII, *infra*. The following Parts III-XVII present the background information necessary to understand the context of the motion for class certification.

III. Anti-Psychotic Medications

Lilly's prescription medicine Zyprexa, with a chemical name of olanzapine, is one of a class of medications known as "atypical" or "second-generation" antipsychotics ("SGAs") that treat schizophrenia and bipolar disease. Schizophrenia is a severe, debilitating mental illness that afflicts over one percent of the general population—2.5 million Americans—often beginning in late adolescence or early adulthood. *See* Robert Freedman, *Schizophrenia*, 349 (18) New Eng. J. Med. 1738, 1738 (2003); Gary D. Tollefson & Cindy C. Taylor, *Olanzapine: Preclinical and Clinical Profiles of a Novel Antipsychotic Agent*, 6 (4) CNS Drug Reviews 303, 304 (2000); U.S. Dep't of Health & Human Servs., Mental Health: A Report of the Surgeon General 273 (1999), http://www.mentalhealth.org/features/surgeongeneralreport/home.asp; DSM-IV-TR, *supra* at 308. One of the most complex and challenging of psychiatric disorders, schizophrenia is a

heterogeneous syndrome of disorganized and bizarre thoughts, delusions, hallucinations, inappropriate affect, and impaired psycho-social functioning. *See* DSM-IV-TR, *supra* at 298-302. The illness occurs when a patient suffers two or more of the following characteristic symptoms: (1) delusions, (2) hallucinations, (3) disorganized speech, (4) grossly disorganized or catatonic behavior, and (5) negative symptoms, *see id.*, or has bizarre delusions or hallucinations of voices commenting on the person's behavior or thoughts. Research has shown a variety of abnormalities in schizophrenic brain structure and function. Pharmacotherapy: A Pathophysiologic Approach (Joseph T. Dipiro et al., eds., 5th ed. 2002) (hereinafter "Pharmacotherapy") at 1219; *see* DSM-IV-TR, *supra* at 299. Causation is believed to be multi-factorial. Pharmacotherapy, *supra* at 121; *see* DSM-IV-TR, *supra* at 305-06, 309-11.

Bipolar disorder is a serious, lifelong mental illness marked by dramatic shifts in mood, from abnormally elevated, expansive, or irritable moods to states of extreme sadness and hopelessness, often with periods of normal mood in between. Nat'l Inst. of Mental Health, Bipolar Disorder, *available at* http://www.nimh.nih.gov/publicat/bipolar.cfm (last visited June 30, 2008); *see* Decl. of Steven Klotz, M.D. 2, Feb. 22, 2007, Docket Entry No. 99 ("Klotz Decl."). Bipolar I, characterized by the occurrence of one of more manic episodes or mixed episodes, often with major depressive episodes, and Bipolar II, characterized by one or more major depressive episodes accompanied by at least one hypomanic episode, are separate disease states. *See* DSM-IV-TR, *supra* at 382-92. Because of its complexity, bipolar disease can be difficult to diagnose; between seven and ten years of mis-diagnoses and incorrect treatment is typical for bipolar patients. Klotz Decl. 6. "[U]ntreated bipolar disorder can be disastrous; 10

percent of sufferers commit suicide." Mary Carmichael, *Welcome to Max's World*, Newsweek, May 26, 2008.

In the past five years there has been extensive research into diagnosing and recommending treatments for bipolar disorder, funded in part by pharmaceutical manufacturers. Klotz Decl. 3. There has been a corresponding growth of bipolar diagnoses—correct *and* incorrect—leading to an increase in patients and greater awareness of the disease; many patients labeled "bipolar" are mentally ill but, upon detailed psychiatric examination, not bipolar. *Id.* at 3-4. An estimated 5.7 million Americans are affected by the disorder.

Both schizophrenia and bipolar disorder, like many mental illnesses, display considerable biological and symptomatic differences. *See* Decl. of Richard G. Frank, Ph.D. at ¶ 7, Jan. 8, 2008, Docket Entry No. 148 ("Frank Decl."). Often, patients with these disorders have other psychiatric and physical problems. *Id.* Due to the illnesses' heterogeneity, different people respond differently to different psychotropic drugs. Which drug will work best for a new patient is often unknown until he or she tries it; thus clinical decision-making about psychotropic medications almost inevitably is based on "trial and error." *Id.* at 3-4 (citing H.A. Huskamp, *Managing Psychotropic Drug Costs: Will Formularies Work?*, Health Affairs 22(5):84-96 (2003)). As a result, third-party payors prefer not to place strong restrictions on the use of antipsychotic medications. *Id.* at 4.

While the two primary uses of second-generation antipsychotics remain the treatment of schizophrenia and bipolar disorder, antipsychotics are prescribed off-label, i.e., for non-FDA approved purposes, to treat symptoms related to agitation, anxiety, psychotic episodes, obsessive behavior, behaviors related to dementia, depression, obsessive compulsive disorder ("OCD"),

Post Traumatic Stress Disorder ("PTSD"), personality disorders, and Tourette's Syndrome. *See* Frank Decl. at 3 (citing Agency of Health Research and Quality, Off Label Use of Atypical Antipsychotic Drugs, *available at* http://effectivehealthcare.ahrq.gov/reports/topic.cfm?topic=8&sid=34&rType=10). "'Off-Label' prescriptions are a mainstay of the drug industry—an estimated 21% of drug use overall." Anna Wilde Mathews & Avery Johnson, *FDA to Propose Guidelines for 'Off-Label' Drug Use*, Wall St. J., Feb. 15, 2008; *see* Rosenthal Decl. 26 (noting that Zyprexa's "unapproved uses represent an average of 31% of Zyprexa mentions in the National Disease and Therapeutic Index (NDTI) database."). Examples of off-label use include using a drug to treat a condition for which it is not indicated, treating an indicated condition with different doses than those specified on the label, and prescribing a drug for a different patient population than that indicated (such as children, if it has only been approved to treat adults). Off-label uses of approved medications have not been subjected to the baseline FDA scrutiny required for on-label indications, and are thus considered riskier. *See id.* at 1021.

Two common off-label uses of SGAs are for dementia in the elderly and children with bipolar disorder. One in four nursing home residents take antipsychotic drugs, with sales in 2007 totaling over $13 billion. Kris Hundley, *Dementia Relief, with a Huge Side Effect: The Off-Label Use of Some Drugs Is Helping*, Tampa Bay Times, Nov. 18, 2007. "The use of antipsychotic drugs to tamp down the agitation, combative behavior and outbursts of dementia patients has soared, especially in the elderly." Tarkan, *supra* at F1. Use of the medications are particularly high in nursing homes. Sedatives and antipsychotics—despite their potentially severe side

effects, including increased risk of death—present a tempting option to overextended staff. *Id.* Of Zyprexa's $4.4 billion sales in 2006, 26.6% were to patients over 64. *Id.*

Off-label use of antipsychotics in children with bipolar disorder is a recent phenomenon. "Between 1994 and 2003, the number of children treated for bipolar disorder in the United States increased to more than 800,000 from 20,000." M. Alexander Otto, *Should Kids Get These Drugs? Plan Likely to Increase Scrutiny of Anti-Psychotics in Children*, News Tribune, May 12, 2008. At least some of those were diagnosed "no doubt . . . wrongly. The disease is hard to pin down." *See* Carmichael, *supra.* Just two SGAs have been approved for use by children, Risperdal and Abilify; Zyprexa is indicated for use by adults only.

A. First-Generation or "Typical" Anti-Psychotics ("FGAs")

Zyprexa is generally known as a "second-generation antipsychotic" or "SGA" to differentiate it from older, first-generation antipsychotics ("FGAs"), which were the standard drug therapy for schizophrenia until the 1990s. FGAs include chlorpromazine (Thorazine), fluphenzine (Proxilin), haloperidol (Haldol), molindone (Moban), thioridazine (Mellaril), loxapine (Loxitane), mesoridazine (Serentil), perphenazine (Trilafon), thiothixene (Navane), and trifluoperazine (Stelazine), some of which have been in use since the 1950s. Pharmacotherapy, *supra*, at 1224. FGAs are sometimes referred to as "typical" antipsychotics and SGAs as "atypical."

Although many different FGAs exist, they share similar levels of efficacy. They are, generally speaking, post-synaptic dopamine-receptor antagonists, i.e., they target dopamine receptors in the brain. *Id.* at 1220. A troubling side effect of typical antipsychotics is that the blockage of dopaminergic neurotransmission causes extrapyramidal syndromes ("EPS") such as

Parkinsonian effects or tremors. *Id.* at 1223. Tardive Dyskinesia ("TD"), a long-lasting movement disorder, frequently occurs with prolonged treatment. *Id.*

B. Second-Generation or "Atypical" Anti-Psychotics ("SGAs")

Because of FGAs' potential for severe side effects and their limited efficacy, many pharmaceutical companies searched for new drugs that would be more effective and cause less movement disorder. By the 1980s, clozapine, the first SGA, was being investigated on that hypothesis. Since it had an "atypical index" when measuring its effect on different parts of the brain, clozapine became known an "atypical" antipsychotic. 2007 Physicians Desk Reference at 2184-89. Clozapine has different effects than FGAs on areas of the brain that control movement; it was hoped that it would cause less movement disorder than other antipsychotics. *Id.* While clozapine turned out to be effective, its toxic side effects, including agranulocytosis (dramatic loss of white blood cells), limited its use to about ten percent of persons with schizophrenia. *Id.*; Decl. of Meredith Rosenthal at 6, Feb. 27, 2007, Docket Entry No. 101 ("Rosenthal Decl."). Although clozapine was the first atypical antipsychotic, it tends to stand on its own between FGAs and SGAs. Clozapine was approved by the FDA in September 1989 and was the only SGA available in the United States until 1993, although its potential toxicity assured only a small market share. *Id.* at Decl. 5. .

During the 1990s pharmaceutical companies, building on the "atypical" hypothesis, developed newer, second-generation antipsychotic drugs ("SGAs") attempting to capture the enhanced therapeutic effect of clozapine without its toxicity and or the side effects caused by traditional antipsychotics, such as EPS and TD. "The introduction of atypical antipsychotic medications was trumpeted by the manufacturers of these pharmaceutical agents as a major

advance in the treatment of schizophrenia with improved symptomatic control of the psychosis and a reduction in both tardive dyskinesia and extra pyramidal side effects." Wirshing Decl. 7.

In late 1993, risperidone became the first non-clozapine SGA to receive Food and Drug Administration ("FDA") approval. In early 1994, Janssen, a subsidiary of Johnson & Johnson, began marketing and selling risperidone under the brand name Risperdal. During the next two years, Janssen heavily marketed and promoted Risperdal for its approved indication, management of the manifestation of psychotic disorders, and, allegedly, for multiple non-approved uses, including attention deficit-hyperactivity disorder, bipolar disorder, and aggression associated with late-onset dementia. By late 1996, Janssen had a significant share of the United States antipsychotic drug market, and had demonstrated the sales potential of marketing SGAs for non-approved indications. When Zyprexa entered the market in 1996, Risperdal was seen as its primary competitor. *See* Strategy Integration Team, Eli Lilly & Co., Zyprexa in Serious Mental Illness (65 Plus Years)—A Strategy Review (undated).

The FDA first approved Zyprexa on September 30, 1996, for use in treating "the manifestations of psychotic disorders" seen in schizophrenia. Letter from Dr. Robert Temple, Director, Office of Drug Evaluation I, FDA, to Dr. Timothy R. Franson, Eli Lilly & Co., Sept. 30, 1996. Thereafter, the FDA approved Zyprexa for maintenance treatment of schizophrenia, FDA Nov. 9, 2000 Approval Letter; for the short-term treatment of acute manic episodes associated with bipolar I disorder as monotherapy, FDA March 17, 2000 Approval Letter; in combination with lithium or valproate, FDA July 10, 2003 Approval Letter; and for maintenance in the treatment of bipolar disorder. FDA Jan. 14, 2004 Approval Letter.

Multiple other second-generation antipsychotic drugs have been introduced since 1996. Atypical SGAs, in addition to clozapine (Clozaril), olanzapine (Zyprexa), and risperidone (Risperdal), now include quetiapine (Seroquel), aripiprazole (Abilify), and ziprasidone (Geodon). Pharmacotherapy, *supra* at 1224. Seroquel has been approved since 1997. Indicated for schizophrenia and acute manic or mixed episodes associated with bipolar disorder, Geodon entered the marketplace in March of 2001, and Abilify in November 2002. Abilify is also approved for treatment of depression. Transcript of Evidentiary Proceedings on Class Certification 827 ("Evid. Hr'g Tr."), March 28, 2008 through April 2, 2008.

C. Rapid Growth of Pharmaceuticals and SGAs

SGAs were and are marketed as providing more effective treatment with fewer side effects and better symptom reduction than the older—and far less expensive off-patent—FGAs. Expert Rep. of John Abramson, M.D., at 7, Feb. 28, 2007, Docket Entry No. 97 ("Abramson Rep."). Because of the severe and costly—in both human and economic terms—nature of the illnesses that SGAs treat, insurance companies, believing the newer drugs to be more effective, have been willing to spend billions of dollars on them, despite the fact that they can cost up to 100 times more than the older antipsychotic medications. *Id.* (noting that, for example, Zyprexa costs more than twenty times the cost of Haldol, an FGA).

In 1994, when Risperdal, the second SGA after clozapine, was introduced, only five percent of schizophrenic patients were being prescribed an SGA; national spending on antipsychotic medications was $1.4 billion. *Id.* Ten years later, about ninety percent of schizophrenic patients nationally were being treated with SGAs rather than FGAs, and $10

billion was spent annually on antipsychotic medications. *Id.*; *see* Frank Decl. 4 (noting that in 2003, IMS Health estimated United States antipsychotic drugs sales to total $8.1 billion).

The dramatic rise in the costs of prescription drugs over the past decade is in large part due to SGAs, which now make up a substantial proportion of increased national spending on medication. In 2004, for instance, prescription drug expenditures in the United States were estimated at $188.5 billion, nearly five times the $40.3 billion the nation spent fourteen years earlier. Prescription Drug Trends, Kaiser Family Foundation (June 2006). "Sales of newer antipsychotics like Risperdal, Seroquel and Zyprexa totaled $13.1 billion in 2007, up from $4 billion in 2000." Tarkan, *supra* at F1; *see* Alex Berenson, *Lilly Adds Strong Warning Label to Zyprexa, a Schizophrenia Drug*, N.Y. Times, Oct. 6, 2007.

SGAs now account for about ninety percent of all antipsychotics drugs prescribed for all psychiatric purposes, regardless of whether they were approved for those indications or not. *See* Jeffrey A. Lieberman, *Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia,* 353 N. Eng. J. of Medicine 1209, 1210 (2005). Off-label prescriptions make up a substantial proportion of overall SGA sales.

Because many patients treated with antipsychotics are severely disabled, Medicare and Medicaid, as public health insurers, are the largest buyers of the drugs. Between 1994 and 2003, total Medicaid spending on all prescription drugs increased by $25.9 billion, quadrupling from $8.4 billion to $34.3 billion; one-third of the increase, $8.5 billion, went towards increased expenditures on SGAs. Abramson Rep. 8. In 2003, three out of the top four drugs that Medicaid purchased were SGAs. *Id.* Zyprexa headed this list: Medicaid paid over $1.8 billion for olanzapine in each of 2003 and 2004, $500 million more than for any other single drug. *Id.*; *see*

CMS Medicaid Drug Utilization data, ranked by Drug, 2003-2006. In 2005, the most recent year for which data is available, Medicaid paid over $1.6 billion for Zyprexa.

D. Lilly, with Zyprexa, Has Been Successful

Zyprexa has been a phenomenal success for Eli Lilly. Approved in more than 80 countries, it has been prescribed to more than 23 million people since 1996. Lisa Demer, *State Claims Drug Maker Hid Data*, Anchorage Daily News, Mar. 6, 2008. Over 73 million Zyprexa and Zyprexa Zydis prescriptions had been written by the end of 2006. *See* Rosenthal Decl., Ex. E.1 (citing IMS Health TRx Data).

From its launch, Zyprexa rapidly cut into Risperdal and Clozaril's market shares, even while the overall market for atypical antipsychotics grew substantially. Rosenthal Decl. 6. For both FDA-approved and off-label indications, Zyprexa has the largest market share for SGAs in the United States, *see* Lieberman, *supra* at 1210, and in 2003, was the seventh best-selling drug in the country with sales of $3.3 billion. Rosenthal Decl. 6. Although 2005 sales dropped to $2.5 billion, *id.*, Zyprexa sales now total $4.2 billion annually. Abramson Rep. 8. During plaintiffs' proposed class period, Zyprexa sales exceeded $22 billion. *See* Pfs.' Mem. in Opp. to Def.'s Mot. for Summary J., June 12, 2007 (filed under seal). In the United States, government payments for Zyprexa totaled $1.5 million in 2007. Alex Berenson, *In Trial, Alaska Says Lilly Concealed Risks of Schizophrenia Drug*, N.Y. Times, Mar. 6, 2008.

Zyprexa now accounts for approximately 27 percent of Lilly's total revenues, down from a high of 33 percent in 2002, *Fitch Affirms Eli Lilly & Co.'s IDR at 'AA'*, Business Wire, Sept. 26, 2007, but constitutes nearly fifty percent of the company's profits. Pretax profits from Zyprexa total $2 billion annually. J.K. Wall, *$2 Billion Challenge: Lilly Under Gun to Replace*

Aging Blockbuster Zyprexa, Indianapolis Business J., Nov. 3, 2007. The average cost per prescription—roughly a month's supply—ranges from $250 to $350. *See* Summary J. Hr'g Tr. 74, June 22, 2007. At commonly prescribed doses, Zyprexa now costs about $8,000 per year. Berenson, *Lilly E-Mail, supra*. Its costs, along with Lilly's profits, is expected to sharply decrease when its patent expires in 2011.

IV. Pharmaceutical Industry

A. Pricing

Unlike those of the typical consumer good, sales of most branded pharmaceuticals are not sensitive to prices or price changes. Such an inelastic market behaves differently from the classic elastic market described by the sloping price and demand curves. Even when there is a wide variation in prices between competing pharmaceuticals, these price differences tend not to affect the unit sales of the products. Especially when a drug treats as serious a disease as a psychiatric disorder, the relative price of an agent has little, if any, affect on product use. Kolassa Decl. 10.

The pharmaceutical market's unique price stability results from the limited monopoly protection afforded by patents, and, where patents have expired, patients' reluctance to switch to generic drugs and physicians and third-party payors' hesitations about requiring such a switch:

> [O]nce launched, prices are unlikely to decline in the face of new warnings or other information because of the presence of brand loyalty. That is, once a drug has been on the market, there will be a segment of patients and physicians that believe that it works for them and will not switch even if significant risks are discovered . . . . When there are significant numbers of brand-loyal customers, a manufacturer in this situation may rationally maintain a high price and capture only the segment of the market that values the product most highly.

Rosenthal Decl. 38-39.

Even when negative information about a medication's safety or effectiveness is released, manufacturers are reluctant to reduce prices; such a move could "signal the market or the courts that the manufacturer accedes to the allegations that the drug is worth less than was initially promised." *Id.* The common result of negative information in sales of branded pharmaceuticals is a decline in quantity, not a decline in price. Quantity declines may thus reflect a reduction in the market's valuation of the drug.

Because of this price rigidity, pharmaceutical companies are able to independently fix and raise their prices routinely. Kolassa Decl 10. Lilly, like other firms, is free to set the price it chooses for its products. *Id.*; Harris Rep. ¶ 17. Competing medicines can somewhat limit a manufacturer's pricing freedom; Zyprexa's price growth, for example, has been consistent and generally paralleled that of most of the other SGAs. Kolassa Decl. 8; *see id.* at tbl. 1.

B. Marketing

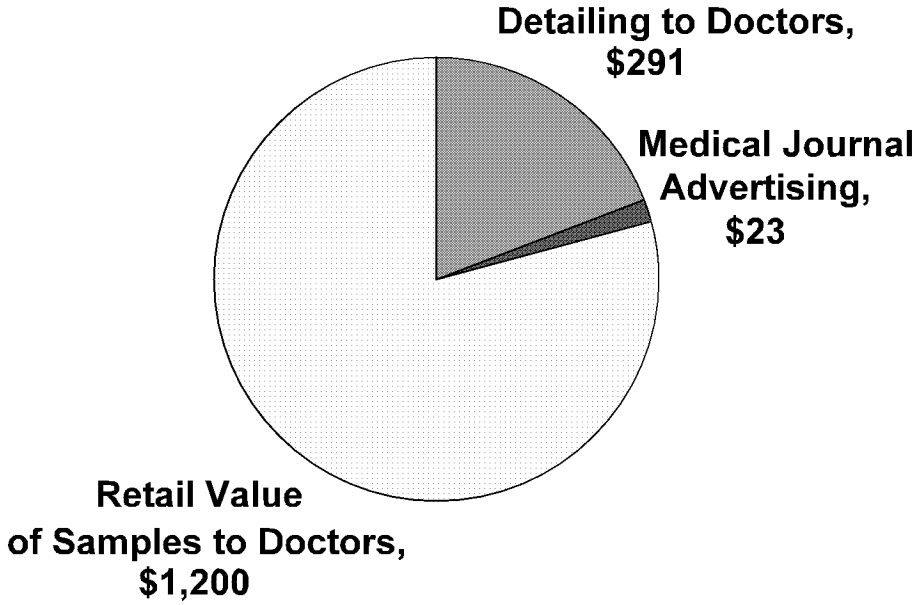
Marketing and advertising have been critical to the success of the pharmaceutical industry in the last two decades. Whether via increasingly common direct-to-consumer ("DTC") advertising or one-on-one physician detailing, drug companies spend billions on advertising. Gardiner Harris, *Group Urges Ban on Medical Giveaways*, N.Y. Times, Apr. 28, 2008; *see also* Rosenthal Decl. 15. In 2000, for example, total national prescription drug promotion expenditures totaled more than $15.7 billion. *See* Adriane Fugh-Berman & Shahram Ahari, *Following the Script: How Drug Reps Make Friends and Influence Doctors*, 4(4) PLoS Medicine 621, 621 (April 2007).

Drug detailing alone accounts for $4.8 billion. *Id.* "Detailing" is the one-on-one promotion of drugs to physicians by pharmaceutical sales representatives, usually through regular

office visits, free gifts, and friendly advice, when "drug reps go to doctors' offices to describe the benefits of a specific drug." Daniel Carlat, *Dr. Drug Rep.*, N.Y. Times. Mag., Nov. 25, 2007, at 67; *see also* Rosenthal Decl. 15. Drug companies hope that drug representatives will increase the sale of a particular drug by influencing physicians with "finely titrated doses of friendship." Fugh-Berman & Ahari, *supra.*

Like many other pharmaceutical campaigns, detailing—including free samples directly distributed to doctors—was the backbone of Lilly's marketing of Zyprexa. Over plaintiffs' putative suggested class period Lilly spent about $291 million on detailing (more than any other SGA) out of a total marketing budget of $1.5 billion, with an additional $1.2 billion going towards drug samples distributed primarily through detailers. *See* Rosenthal Decl. 25. Its Zyprexa sales representatives wrote over fourteen million call notes, each describing doctor interactions; Evid. Hr'g Tr. 744 (Abramson testimony); two thousand detailers were employed just for the primary care market alone. (Unlike many drug manufacturers, Lilly never condescended to advertising and marketing its drug directly to gullible lay consumers through maddeningly battological television and other media. *Id.* at 832-33 (Cockburn testimony).) The below chart and table illustrates Lilly's overall promotional spending on Zyprexa from 1996 through 2006.

Total Zyprexa Promotional Spending, 1996-2006 ($ millions)



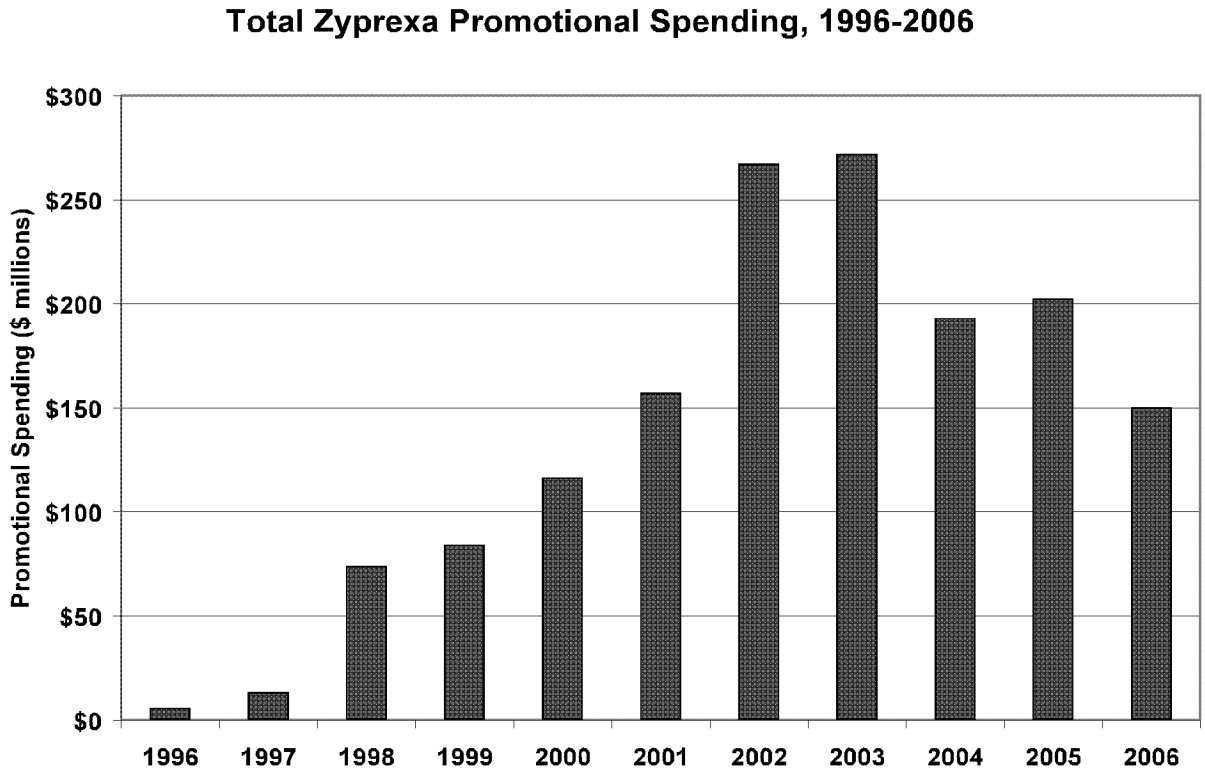
Pfs. Corr. Response 340.

Lilly's expensive promotional effects were driven by a sense of urgency: with its patent for former bestseller Prozac running out, Zyprexa's success was crucial to Lilly's future. *See* Elizabeth Lopatto & Allan Dodds Frank, *Lechleiter, Replacing Taurel as Lilly Chief, Pushes Pipeline*, Bloomberg.com, Dec. 19, 2007, http://www.bloomberg.com/apps/news?pid=20601087&sid=aKo2Xxlu2bNg&refer=home ("Prozac generated $2.6 billion in annual sales before a U.S. appeals court stripped the drug of patent protection in 2001."). In 1995, Lilly valued the market for schizophrenia drugs at $1 billion, but believed it to have "the potential to be an estimated $3.5 billion market by 2000,"

possibly reaching $6 billion by 2006. Eli Lilly & Co., Zyprex [sic]—A Major Step Forward Toward a Health Care Solution for Psychosis, July 20, 1995, at 12.

Zyprexa's promotional expenditures began low, then rapidly increased until 2003, when they dropped almost as quickly. At the peak in 2003, Lilly spent approximately $275 million per year marketing Zyprexa, declining to $150 million by 2006. Spending on detailing peaked earlier, at $60 million in 2001, although its effects lasted for some time longer. (The "stock of detailing" can be thought of as slowly accumulating, and then depreciating, over time. Evid. Hr'g Tr. 889 (Cockburn testimony). Promotional effects are long-lived; once physicians and or patients are motivated to try a drug, they tend to stay with it. Rosenthal Decl. 20-21.)

The table and graph below, based on IMS Health data, show Lilly's total promotional spending as well as its combined expenditures on Zyprexa detailing and sampling alone, broken down by year.



Year	Combined Nominal Expenditures on Detailing and Sampling of Zyprexa ($millions)
1998	71.5
1999	82.2
2000	114.1
2001	151.6
2002	262.4
2003	256.2
2004	177.5
2005	194.1
2006*	170.2

Harris Rebuttal 11 tbl. 1.

*Projected to full year, based on first 10 months.

Lilly's advertising and detailing budget was not unusual. Other companies spent similar amounts promoting their SGAs. Detailing expenditures for Abilify, for example, have risen to at least $40 million, Evid. Hr'g Tr. 831 (Cockburn testimony); its DTC advertising budget in 2001 totaled about $40 million per quarter. *Id.* at 832-33.

C. Wholesale Influence of Drug Marketing

It is undisputable that expenditures for drug marketing increase sales. The billions spent by the pharmaceutical industry attests to that. Physicians, despite what most claim, *are* influenced both consciously and unconsciously by commercial promotional messages. Scientific knowledge and judgment are not impervious shields against fraudulent product claims. Rosenthal Decl. 18; *see id.* at 16 (noting recent studies demonstrating that "despite their extensive training, physicians are influenced by marketing messages even when they are flawed or contradicted by scientific evidence."). One study, for instance, showed that the majority of doctors held beliefs about two classes of drugs that were consistent with the detailing message

but at odds with the scientific evidence, even though the same physicians reported that commercial sources of information had little influence on their prescribing. *Id.* at 17 (also noting that doctors deny that gifts and payments have any effect on their own prescribing behavior).

The medical community appears to be only beginning to grasp the extent and influence of pharmaceutical companies over the medical system and prescribing decisions. According to the American Medical Student Association, most medical schools do not adequately restrict the money, gifts, and free drug samples that drug companies routinely provide doctors and trainees. Gardiner Harris, *Survey of Medical Schools Is Critical of Perks*, N.Y. Times, June 3, 2008, at A20. A new model policy by the Association of American Medical College governing interactions between medical schools and the drug industry "recommend[s] that gifts of free food and gifts to students and teachers be banned and that schools discourage faculty involvement in industry-sponsored speakers' bureaus." Harris, *Group Urges Ban, supra.* Even Congress has taken notice: a proposed bill, the Physician Payments Sunshine Act would require the pharmaceutical industry to report gifts, payments, travel reimbursements and donations over $500 to the medical field—but exempts product samples, training and educational opportunities; the bill has been endorsed by Lilly. Daniel Barlow, *State: U.S. Bill Would Undermine* [*Vermont*] *Drug Maker Gift Rules*, Rutland Herald, May 27, 2008.

Intense pharmaceutical marketing saturates the industry and appears in many forms—some of which could be characterized as disguised. Lilly's marketing efforts are central to plaintiffs' allegations. To support their claims that as soon as Zyprexa launched, Lilly began a pattern of misleading the public and the healthcare community, minimizing the known side effects of the drug and overstating its efficacy as well as fraudulently and illegally promoting it

for off-label use, plaintiffs point to evidence that Lilly utilized all the various channels of information through which pharmaceutical companies can market their products to propel Zyprexa's brand message. *See* Part XVIII.A.6, *infra* (testimony of plaintiffs' expert Dr. Abramson); *see, e.g.*, Lisa Demer, *Defense Opens in Zyprexa Trial*, Anchorage Daily News, Mar. 22, 2008 (reporting that David Kahn, a professor of psychiatry at Columbia University Medical Center and a defense witness for Lilly in the Alaska trial, confirmed during his testimony that there is no source of information in which Lilly is not involved); Sheri Qualters, *Drug Makers Look at New Ethics Code*, Nat'l L.J., Aug. 4, 2008 (reporting the Pharmaceutical Research and Manufacturers of America's ("PhRMA") massive overhaul of its ethics code governing interactions with health care professionals to restrict marketing by limiting free meals and banning certain gifts, institute strict protocols for speaking and consulting arrangements, and train sales representatives on laws, regulations, and industry codes; emphatically endorsed by the U.S. Department of Health and Human Services, it will probably be implemented by Lilly starting next year). Those channels—today highly susceptible to industry influence—are described below.

1. Drug Labels

The most obvious source of information about a medication is its own prescription label. Abramson Rep. 9. "[L]abels are the primary means of providing prescribing physicians and their patients with important information on a drug's risks and benefits." Karen Baswell, Note, *Time for a Change: Why the FDA Should Require Greater Disclosure of Differences of Opinion on the Safety and Efficacy of Approved Drugs*, 35 Hofstra L. Rev. 1799, 1803 (2007). Approved indications and respective dosage information appear on the label. 21 U.S.C. §§ 352, 355(d).

Although a pharmaceutical company must obtain the FDA's approval for its drug's label, the label is the property of the manufacturer, not the FDA. *Id.* Initially drafted by the manufacturer, labels are then subject to negotiations between the federal agency and the manufacturer. *Id.* Because the FDA depends solely on drug safety and efficacy information provided by pharmaceutical companies, it cannot effectively object to a label's shortcomings if it never received the data from the manufacturer showing the drug's drawbacks. *See* Part V, *infra.*

2. Clinical Trials

Clinical trials provide the empirical data upon which the FDA determines a drug's safety and efficacy and doctors make professional judgments about the relative risks and benefits of a drug—and whether it is appropriate to prescribe it for their patients. The pervasive commercial bias found in today's research laboratories means studies are often lacking in essential objectivity, with the potential for misinformation, skewed results, or cover-ups. One of the plaintiffs' experts described how he saw this situation:

> [C]orporate influence now permeates every aspect of this process, from the design of clinical studies (including the population included in the trial, the choice of drugs, doses, and duration of the trial, and the outcome and safety measures to be tracked), to control of the data, data analysis, the writing of manuscripts for articles, and publication decisions.

Abramson Rep. 14.

Such bias is a recent phenomenon. Before 1980, the National Institute of Health ("NIH") funded most clinical trials. During the 1980s, its budget was slashed; in response, drug industry funding went up six-fold from 1977 to 1990. *Id.*; Evid. Hr'g Tr. 722. By 1991, drug companies funded 70% of all clinical trials, though 80% of commercially funded trials were still performed at universities. Abramson Rep. 14; Evid. Hr'g Tr. 723. By 2004, only 26% of commercially

funded trials took place at universities. Abramson Rep. 15. Today 80% to 90% of all trials are commercially funded, *id.*; between 66% and 75% of the clinical studies published in the most prestigious medical journals are commercially funded. *Id.* at 16. Study design and control are increasingly in the hands of drug companies. Evid. Hr'g Tr. 727. Published studies often do not reflect their commercial ties or authorship; they may be "ghostwritten" by company employees, use proprietary data not accessible to the scientific community, or simply fail to acknowledge their authors' financial ties to drugmakers. *See e.g.*, Rob Waters, *Harvard Doctors Failed to Disclose Fees, Senate Says*, Bloomberg.com, June 9, 2008 (reporting that Harvard Medical School doctors who helped pioneer the use of psychiatric drugs in children violated federal and school rules by failing to disclose at lease $3.2 million from drug makers, including Lilly); Editorial, *Hidden Drug Payments at Harvard*, N.Y. Times, June 10, 2008, at A22.

Sponsorship is not insignificant. *Cf. Exxon Shipping Co. v. Baker*, 128 S. Ct. 2605, 2626 n.17 (2008) ("Because this research [supporting defendant Exxon's position] was funded in part by Exxon, we decline to rely on it."). Even those trials performed at academic institutions are often partly to almost wholly controlled by the sponsor. *See* Abramson Rep. at 15. Sponsorship significantly increases the chance of positive results; the odds are 5.3 times greater that commercially funded studies will conclude that the sponsor's drug is the treatment of choice compared to non-commercially funded studies of exactly the same drug. Evid. Hr'g Tr. 724; Abramson Rep. 16. Odds of a trial favoring a drug also greatly increase if the trial's researchers had a financial conflict of interest with a manufacturer. Abramson Rep. 18. "For those studies that had both industry sponsorship and at least one author with a conflict of interest the odds were 8.4 times higher that the study would favor the sponsor's drug." *Id.*

Not only does commercial bias affect the probable outcome of a study, it also often controls whether and when a study is published. Because drug manufacturers often delay or suppress negative results from clinical trials they or their affiliated research institutions conduct, "doctors, formulary committees, and policy makers [may base] their decisions on an unrepresentative fraction of the available scientific evidence." *Id.* at 19 (giving the example that when such authorities opined on the safety of antidepressants for children, only six out of a total of fifteen completed studies had been published); *see* Benedict Carey, *Researchers Find Bias in Drug Trial Reporting*, N.Y. Times, Jan. 17, 2008, at A20 ("The makers of antidepressants like Prozac and Paxil never published the results of about a third of the drug trials that they conducted to win government approval, misleading doctors and consumers about the drugs' true effectiveness, a new analysis has shown."); Alex Berenson, *Accusations of Delays in Releasing Drug Results*, N.Y. Times, Apr. 1, 2008, at C7 (reporting a lead investigator's allegations that his study's commercial sponsor deliberately delayed for two years the release of his trial results, which reflected negatively on the sponsor's drug, "to hide something."); *cf.* Alan Finder, *At One University, Tobacco Money Is Not Taboo*, N.Y. Times, May 22, 2008, at A29 (reporting that the Virginia Commonwealth University's formerly secret 2006 contract with Philip Morris for tobacco research gives the company the sole power to decide whether to publish by defining all university-created material as its proprietary information).

3. Journal Articles

Clinical trials are made public via research and review articles in medical journals. Doctors value keeping up-to-date with medical literature, and journal articles are their primary source of best practices and current developments. Evid. Hr'g Tr. 721, 718. Research articles

describe individual primary clinical trials; review articles summarize results from multiple trials on the same subject. *Id.* at 721. Both are subject to systemic industry bias. Abramson Rep. 20. Because of the increase in commercially-funded trials, the number of commercially funded journal publications has likewise dramatically increased. Today, two-thirds to three-quarters of trials published in the four most respected medical journals are commercially funded. *Id.* at 725; Abramson Rep. 16. Several editors of preeminent medical journals have gone so far as to say that their publications "have devolved into information-laundering operations for the pharmaceutical industry." *Id.* at 728; Abramson Rep. 20. For example, by April 16, 2002, the Zyprexa product team had published 125 full manuscripts and submitted an additional 100 for publication. Evid. Hr'g Tr. 731.

4. Drug Detailing

As discussed above in Part IV.B, medical detailing is a large field, employing over 90,000 sales representatives, or one detailer for every 4.5 doctors. Abramson Rep. 10. The vast majority of doctors—eighty-five to ninety percent—speak with drug detailers, and most consider them and the information they provide helpful and accurate. Evid. Hr'g Tr. 743; Abramson Rep. 10. Drug representatives ostensibly provide useful information for physicians since they address "difficult problems in treating patients." Jonna Perala et al., *Lifetime Prevalence of Psychotic and Bipolar I Disorders in a General Population,* 64 Archives of Gen. Psychiatry 19, 1892 (2007).

But company-controlled and produced information has great potential to mislead: one Journal of General Internal Medicine article "shows that nearly half (forty-two percent) of the material given to doctors by drug reps made claims in violations of FDA regulations. And only thirty-nine percent of the material provided by drug reps provided scientific evidence to back up

claims." Abramson Rep. 25. Pharmaceutical sales representatives are prohibited from promoting off-label uses; they may legally only provide information about off-label uses if a physician specifically requests the information. *See* Part V.C, *infra*. In the present case, plaintiffs make extensive allegations of Lilly's misleading and extensive off-label detailing. *See, e.g.*, Part IX.A, *infra*.

5. CME Course and "Thought Leaders"

Another key source of drug information for doctors is continuing medical education ("CME") courses, usually medical lectures held locally featuring prominent "thought leaders" as speakers. *See id.* at Rep. 21-22; Schneider Rep. 12. Required to maintain medical licenses and to stay current with new developments to give patients the best medical care, many CME courses provide expert syntheses of clinical trial information. Evid. Hr'g Tr. 735-36.

Like clinical trials themselves, the percentage of CMEs that are commercially funded has increased sharply, from 48% in 1998 to 58% in 2002. Abramson Rep. 22; *see* Evid. Hr'g Tr. 736. Sixty percent of CMEs have direct commercial sponsorship; indirect sponsorship (e.g., via non-profits funded by company money) accounts for a large portion of the remainder. Total industry contributions towards continuing medical education is estimated to be 70% or higher and in the hundreds of millions of dollars. Abramson Rep. 22 (noting that commercial sponsorship grew from $400 million in 1998 to $700 million in 2002).

Lecture fees are used to recruit recognized clinical experts, well-known and respected in their field and referred to as "thought leaders" or "key opinion leaders," to join company "speakers bureaus" and conduct CMEs. *Id.* at 21. "[O]ne recent study indicates that at least 25 percent of all doctors in the United States [approximately 200,000 physicians] receive drug

money for lecturing to physicians or for helping to market the drugs in other ways." Carlat, *supra,* at 67; *see also* Gina Kolata, *Citing Ethics, Some Doctors Are Rejecting Industry Pay*, N.Y. Times, Apr. 15, 2008 (reporting that a small number of prominent academic scientists have decided to stop accepting payments from food, drug and medical device companies in response to accusations of ethical conflicts inherent in these arrangements). In many of these presentations, the slides used have been "created by drug makers, not the speakers. That's like ghost-talking." Harris, *Group Urges Ban, supra*; *see id.* ("Speakers' bureaus and drug samples are pillars of the industry's marketing operations").

Studies have shown that commercial sponsorship does result in biased CMEs. Evid. Hr'g Tr. 737; *see* Abramson Rep. 10. "Drug company-sponsored lectures are two-and-a-half to three times more likely to mention the sponsor's drug in a positive light and the competitors' drugs in a neutral or negative light than are non-commercially sponsored lectures." *Id.* at 22-23. Increased formulary requests, the prescribing of new brand-name drugs instead of older generic products, and the prescribing of the specific product promoted have all been demonstrated to increase after exposure to pharmaceutical promotion and company-sponsored CMEs. *See id.* at 26 (effect of drug detailing).

6. Clinical Practice Guidelines and Nonprofit Organizations

Clinical Practice Guidelines ("CPGs") are an important source of drug information for physicians. Evid. Hr'g Tr. 765-66. Summarizing expert opinions and often used to identify the standard of care, CPGs are closely followed by prescribers, who prefer not to depart from the identified standards to avoid charges of medical malpractice. Abramson Rep. 25-26. Guidelines are typically formulated by panels of experts under the auspices of quasi-governmental

organizations, medical professional societies, or non-profit organizations like the National Alliance of the Mentally Ill ("NAMI"), the American Psychiatric Association ("APA"), and the Texas Medication Algorithm Project ("TMAP"). Abramson Rep. 68 ("Guidelines and algorithms advanced by these organizations have a significant effect on the standard of care and the prescribing decisions of doctors.").

Such entities "have been particularly active in promoting treatment of the mentally ill with atypical antipsychotics." *Id.*

> A host of practice guidelines and algorithms drafted before the publishing of many of the recent, independent studies on atypical antipsychotics advanced the idea that SGAs should be used as first line treatment for schizophrenia and bipolar disorder. For example, the Expert Consensus Guideline Series, Treatment of Schizophrenia 1999 recommended SGAs for first line treatment, acute exacerbation, failure of FGA at low doses, and failure of another SGA. The American Psychiatric Association instituted the second edition of its Practice Guideline for the Treatment of Patients with Schizophrenia in 2004 and recommended SGAs as first line treatment for patients in the acute phase of schizophrenia. The Texas Medication Algorithm Project ("TMAP") recommend[ed] SGAs rather than FGAs for Stage 1 and 2 of antipsychotic treatment.

Id. at 68 (footnotes omitted). (In November 2007, TMAP reversed its earlier position on the basis of recently published studies and issued a revised consensus judgment by leading experts suggesting that there is no advantage for chronic schizophrenics of SGAs over FGAs. *See* Rosenheck Supp. Decl. 7.)

Many organizations are partially or fully financially supported by pharmaceutical manufacturers. *Id.* at 26. NAMI, for instance, received $544,500 from Lilly in the first quarter of 2007. Avery Johnson, *Under Criticism, Drug Maker Lilly Discloses Funding*, Wall St. J. Online, May 1, 2007, http://online.wsj.com/article/SB117798677706987755.html. And panel experts often have economic ties to the industry via research grants or speaker fees. Every single

expert, for example, who worked on the sections devoted to severe mental illness, including schizophrenia, in the 1994 edition of the DSM-IV, the APA's most important diagnostic handbook, had financial links to drug makers; more than half the task force members who will oversee the next edition have such connections. Tara Parker-Pope, *Psychiatry Handbook Linked to Drug Industry*, N.Y. Times Blog, May 6, 2008, http://well.blogs.nytimes.com/2008/05/06/psychiatry-handbook-linked-to-drug-industry/.

V. Role of the Food and Drug Administration

A. Approval Process

Under the Food, Drug, and Cosmetics Act ("FDCA"), new pharmaceutical drugs cannot be marketed in the United States unless the sponsor of the drug demonstrates to the satisfaction of the FDA that the drug is safe and effective for each of its intended uses. 21 U.S.C. §§ 355(a), (d). A drug receives FDA approval only for treatment of specified conditions, referred to as "indications." 21 U.S.C. §§ 352, 355(d). For each indication sought a manufacturer must provide condition-specific safety and efficacy information. *Id.* The FDA also determines the particular dosage (or range of dosages) considered safe and effective for each indication.

To determine whether a drug is "safe and effective," the FDA relies on information provided by a drug's manufacturer; it does not conduct any substantial analysis or studies itself. Applications for FDA approval (known as New Drug Applications or "NDAs") must include "full reports of investigations which have been made to show whether or not such drug is safe for use and whether or not such drug is effective in use." 21 U.S.C. § 355 (b)(1)(A). FDA approval of prescription drugs is wholly dependent upon the accuracy of information provided by drug manufacturers. *See* Abramson Rep. 11. *See generally* Wayne A. Ray & Michael Stein, *Reform*

of Drug Regulation—Beyond an Independent Drug-Safety Board, 354(2) New Eng. J. Med. 194 (Jan. 12, 2006).

Not only does the FDA depend upon industry-supplied data, but it also relies on direct financial support from the industry. "By law, makers of brand-name drugs pay application fees to the F.D.A. in exchange for the agency's commitment to act within 180 days." Bloomberg News, *F.D.A. Revises Its Letter for Nonapproval of Drugs*, N.Y. Times, July 10, 2008. "[S]ince the enactment of the Prescription Drug User Fee Act of 1992 . . . the pharmaceutical industry provides between twenty to fifty percent of the funding for the FDA's activities. The regulating agency is therefore dependent on those it is supposed to be regulating." Baswell, *supra* at 1828.

As a result, some have alleged that the FDA and the pharmaceutical industry have many close ties:

> [F]ederal drug policy seems to currently favor the commercial pharmaceutical industry. Differences of opinion regarding drug safety and efficacy in a new drug application seem to be decided in favor of the manufacturer (at least initially). After approval, challenges to a drug's safety or to the adequateness of the drug's label regarding risks are seemingly set aside until the effects of the risks become so egregious that the manufacturer or the FDA is forced to address them. This set-aside period allows the manufacturer to maximize profits before removing either an indication for a drug or the drug itself.

Id. at 1829; *see also* Gardiner Harris, *Potentially Incompatible Goals at F.D.A.: Critics Say a Push to Approve Drugs Is Compromising Safety*, N.Y. Times, June 11, 2007, at A14 (reporting that "several F.D.A. safety reviewers in recent years have been punished or discouraged after uncovering . . . drug dangers").

FDA approval does not require that a new drug be more effective or safer than other drugs approved to treat the same condition. Neither does it require that the drug be cost-

effective. *See* Robert Rosenheck, *The Growth of Psychopharmacology in the 1990s: Evidence-Based Practice of Irrational Exuberance*, 28 Int'l J. Law & Psychiatry 467 (2005). A drug must only be shown to be more effective than a placebo in treating a particular condition and be without any statistically significant adverse safety findings. *See* Abramson Rep. 11-13; Ray & Stein, *supra*, at 194. Comparative data showing performance as against that of existing drugs is not required; the FDA has no basis for determining that one drug is better than another drug. *See* Ray & Stein, *supra*, at 194.

Because short-term studies are accepted, drug applications often do not contain long-term data on the safety or efficiency of the drug. Abramson Rep. 11. Approval of a new drug generally contains a requirement that the manufacturer pursue further long-term studies, but two-thirds of the promised studies never materialize and the FDA lacks any enforcement authority. *Id.* at 12-13. Many of the effects of newly approved drugs could not possibly be known at the time of FDA approval, particularly the long-term effects of taking a medication, given the short length of, and relatively few participants in, the clinical trials conducted for approval. *See AP Analysis: How a Drug's Risks Emerge*, N.Y. Times, May 23, 2007. There is no systematic provision requiring drug companies to conduct—or provide results from—post-marketing studies. *Id.*

A manufacturer wishing to market an approved drug for indications other than those already approved must resubmit the drug for a series of clinical trials similar to those required for the initial FDA approval. *See* Food and Drug Administration Modernization Act of 1997 ("FDMA"), 21 U.S.C. §§ 360aaa(b), (c); *see also* 21 C.F.R. § 314.54 (outlining the administrative procedure for filing an application for a new indication); 21 U.S.C. §§ 301 *et seq.*

A supplemental NDA must be filed. Unless and until an additional indication is approved by the FDA, the unapproved use is considered to be "off-label."

As the primary gatekeeper of drugs with potentially life-saving or life-changing effects, the FDA often finds itself between a rock and a hard place: "Safety and speed are the yin and yang of drug regulation. Patients want immediate access to breakthrough medicines but also want to believe the drugs are safe. These goals can be incompatible." Harris, *Potentially Incompatible Goals*, *supra* at A14.

B. Drug Labeling

Critical for conveying a drug's approved uses and known warnings to prescribers, a drug's labeling must also be approved by the FDA as part of the original application. "Labels" include all marketing and promotional materials relating to the drug as well as the printed insert included in its packaging. They may not describe intended uses for the drug that have not been approved by the FDA. 21 U.S.C. §§ 331, 352.

Manufacturers and the FDA typically negotiate over the wording and content of the label, especially in regards to adverse information about the drug. The FDA aims to strike a balance between too-strong warnings, which may scare away patients who would substantially benefit from the drug, and inadequate warnings, which can lead patients incurring injurious side effects. *See, e.g.*, Benedict Carey, *Caution, Not Panic, Seen After Drug Warnings*, N.Y. Times, Jan. 8, 2008, at F6 (reporting that a new study has found that recent suicide warnings on anti-depressants have "seemed to prompt caution rather than panic.").

After a drug is approved, the FDA continues to exercise control over the product's labeling. To protect patients from safety concerns, the FDA may require a label change to reflect

the increased risk of various side effects or interactions, restrict a drug's indications, or, in extreme cases, force a withdrawal from the market. *See* 21 C.F.R. § 201.57(3); Abramson Rep. 13. Negotiation over proposed modifications is common, *see* 21 U.S.C. § 355(d); Ray & Stein, *supra*, at 194-95, and compromise often results. *See* Raymond L. Woosley, *Drug Labeling Revisions—Guaranteed to Fail?*, 284(23) JAMA 3047 (Dec. 20, 2000); *see, e.g.*, Part XI, *infra*. A manufacturer may independently change its product label upon learning new safety information.

C. Drug Marketing, On and Off-Label

FDA regulations restrict how drug companies may market and promote approved drugs. *See* 21 U.S.C. §§ 331, 352; 21 C.F.R. § 314.81. The FDA's Division of Drug Marketing, Advertising and Communications ("DDMAC") is charged with overseeing the marketing and promotion of FDA-approved drugs to ensure that advertisements are not false or misleading, provide a fair balance between the benefits and risks of the drug, and do not promote "off-label" uses. *See* Statement by Janet Woodcock, M.D. (Director, Center for Drug Evaluation and Research ("CDER"), FDA) Before the Senate Special Committee on Aging.

Promotional materials, both professional- and consumer-oriented, must be consistent with the FDA-approved product labeling. Rosenthal Decl. 15. Only claims that are supported by scientific evidence (according to strict scientific procedures) and which are not false or misleading may be asserted by drug companies. *Id.* FDA oversight is supposed to ensure a "fair balance" in all marketing claims and materials, *id.*; its regulations require that the risks as well as the benefits must be clearly identified and given appropriate prominence. *Id.* at 14-15; *see, e.g.*, Part VI.D, *infra*. This restriction pertains to the clinical indications for which the drug has been

approved as well as the dosing regimen that is supported by the clinical trials that were undertaken to establish safety and efficacy. Rosenthal Decl. 14-15. Illegal "misbranding" or encouragement of off-label use can result in criminal penalties. *See* 21 C.F.R. § 333. The Justice Department has reached a number of legal settlements, for example, with drug companies accused of such illegal marketing. Mathews & Johnson, *supra*.

In general the FDA's effectiveness in regulating drug promotion is limited. In 2003, DDMAC's entire staff consisted of forty members, with twenty-five reviewers responsible for reviewing all pharmaceutical advertisements and promotional materials. *Id.*; Abramson Rep. 12. Moreover, such materials do not have to be pre-approved; FDA review of promotional materials occurs, if it does at all, after the materials have already appeared in public. Woodcock Statement, *supra*. Upon finding a violation, DDMAC generally requests, but does not require, the company to stop using the promotional materials. *Id.*; Andrew Eder, *AstraZeneca Defends Drug's Soaring Sales*, Delaware Online, Aug. 3, 2008 (reporting that "a recent report by the Government Accountability Office found that when FDA finds a drug company promoting an off-label use, it takes the agency an average of seven months to issue a warning, followed by four more months for the company to fix the problem"); *see, e.g.*, Part VI.D, *infra*. *But cf* "There's Danger Here, Cherie!" Richard C. Ausness, *Liability for the Promotion and Marketing of Drugs and Medical Devices for Off-Label Uses*, 73 Brook. L. Rev. 1253 (2008) (arguing that more off-label use should be recognized by governmental agencies). Sponsors occasionally are required to publicly correct product misimpressions created by false, misleading, or unbalanced materials. Woodcock Statement, *supra*.

Any use of an approved drug for a purpose other than those indicated in the labeling, whether for a different population, medical condition, or dosage, is considered to be "off-label." *Buckman Co. v. Plaintiff's Legal Committee*, 531 U.S. 341, 350 (2001); *see* David C. Radley, *Off-Label Prescribing Among Office-Based Physicians*, 166 Archives of Internal Medicine 1021 (May 8, 2006). Physicians may prescribe drugs for off-label uses at their discretion. *See* 21 U.S.C. § 396; *Sita v. Danek Medical Inc.*, 43 F. Supp. 2d 245, 263 (E.D.N.Y. 1999) ("[D]octors commonly exercise professional medical judgment and prescribe drugs for uses not within the indications articulated by the FDA."); Gregory J. Radomisli, *Liability for Off-Label Use*, N.Y.L.J., June 20, 2008, at 4 (discussing doctors' freedom to prescribe off-label and quoting *Buckman* and *Sita*). It is generally agreed that "off-label prescribing can benefit both individual patients and patient populations as clinical experience leads to the formation of hypotheses to be tested in structured clinical trials." Rosenthal Decl. at 11. As one of plaintiffs' experts testified,

> The lack of an indication in the label should not be an issue, however, in the concerned physician's managing of patients and prescribing a medication "off-label." Physicians and the community recognize that many drugs effective for a condition may not be labeled for that condition and may not have a strong body of evidence for or against their use. When considering off-label prescribing, physicians depend on the patient-specific evidence they have available to them. This includes the particular patient, the severity of his problems, the successfulness of prior treatment, and the risks of not treating.

Schneider Decl. 11-12.

There are loopholes to prohibitions against off-label promotion. Off-label information may be distributed by sales representatives if requested by a health care provider. 21 U.S.C. §§ 360aaa-366. "[D]octors may freely discuss off-label uses with other doctors at continuing medical education events, which are often sponsored by drug makers." Eder, *supra*. In a move

welcomed by the drug industry, the FDA is now developing guidelines on how drug and medical-device manufacturers can provide doctors with reprints of medical journal articles that deal with uses of drugs and devices that have not won FDA approval. Mathews & Johnson, *supra*.

D. Monitoring of Adverse Side Effects

Once a drug has been approved, the FDA's statutory authority is limited to requesting label changes, negotiating restrictions on distribution with the manufacturer, and petitioning for the withdrawal of the drug from the marketplace. Ray & Stein, *supra*, at 195. Title 21 of the Code of Federal Regulations requires that "as soon as there is reasonable evidence of a serious hazard with a drug," the "Warnings" section of the label should be revised accordingly. "Special problems, particularly those that may lead to death or serious injury, may be required by the Food and Drug Administration to be placed in a prominently displayed box," 21 C.F.R. § 201.57 (e), commonly known as a "black box" warning.

The FDA's Office of Surveillance and Epidemiology ("OSE") is responsible for overseeing the safety of approved drugs. Abramson Rep. 12. Like DDMAC, OSE is underfunded and understaffed. *Id.* For example, "[t]he F.D.A. has 200 inspectors, some of whom audit clinical trials part time, to police an estimated 35,000 testing sites." Gardiner Harris, *Report Assails F.D.A. Oversight of Clinical Trials*, N.Y. Times, Sept. 28, 2007, at A1; *see* Gardiner Harris, *Advisers Say F.D.A.'s Flaws Put Lives at Risk*, N.Y. Times, Dec. 11, 2007, at A12 (reporting on an FDA Advisory Board's conclusion that the "FDA is falling further and farther behind in carrying out its responsibilities and understanding the science it needs to do its many jobs."); Gardiner Harris, *Report Assails F.D.A. Oversight of Clinical Trials*, N.Y. Times, Sept. 28, 2007, at A1 (noting another government report's conclusion that "the agency's

oversight of clinical trials is disorganized and underfinanced . . . . [F]ederal health officials did not know how many clinical trials were being conducted, audited fewer than 1 percent of all testing sites and, on the rare occasions when inspectors did appear, generally showed up long after the tests had been completed."); *cf.* Marcia Coyle, *FDA-Regulated Officials Face Tougher Penalties*, Nat'l L.J., May 12, 2008, at 7 ("Underfunded, undermanned and under criticism for its enforcement effort in recent years, the agency has sought a broad range of [sentencing] guideline changes which, if approved, would have stiffened sentences dramatically . . . . 12 years ago, the FDA sought wholesale revisions to the guideline covering nonfraud violations of the FD&CA, but the [sentencing] commission withdrew the proposals after negative industry reaction."); Gardiner Harris, *Tainted Drugs Put Focus on the F.D.A.*, N.Y. Times, Mar. 17, 2008, at A13 (discussing recent deaths from tainted heparin produced in China and the FDA's inability to conduct inspections of foreign manufacturing plants); Barry Meier, *Calling for a Warning System on Artificial Joints*, N.Y. Times, July 29, 2008, at A1 (FDA's ability to monitor medical devices overwhelmed). *See also* Gardiner Harris, *More Money for Food Safety Is Sought: After Outbreak of Salmonella, Department Asks for $275 Million*, N.Y. Times, June 10, 2008, at A17.

Although drug companies are under a continuing obligation to report serious adverse events, with required safety reports to be filed every three months during the first few years of marketing of a drug, the FDA's adverse event reporting system is largely voluntary. *See* Phil B. Fontanarosa et al., *Postmarketing Surveillance—Lack of Vigilance, Lack of Trust*, 292 JAMA 2647, 2647 (2004). There was some evidence presented at the evidentiary hearing that a major problem with this country's system of ensuring postmarketing drug safety is that it is "the drug

makers themselves who are largely responsible for collecting, evaluating and reporting data from postmarketing studies of their own products." Abramson Rep. 13 (quoting Fontanarosa, *supra*). Drug companies have an incentive to minimize reporting.

Through the FDA's Safety Information and Adverse Event Reporting Program ("MedWatch"), consumers and healthcare professionals may voluntarily report "serious problems that they suspect are associated with drugs." What is MedWatch?, FDA MedWatch Homepage, http://www.fda.gov/medwatch/What.htm (last visited July 12, 2008); *see* Gardiner Harris, *F.D.A. to Expand Scrutiny of Risks from Drugs After They're Approved for Sale*, N.Y. Times, May 23, 2008, at A17 ("The agency now relies on an unsystematic system in which doctors, patients, and manufacturers report problems with drugs and medical devices when they deem them important. . . . The agency estimates that it receives reports for only a fraction of actual drug effects"). *But see id.* (reporting on the FDA's announcement of a new "Sentinel Initiative" system to allow officials to monitor drug safety using Medicare claims data).

Health care professionals are not required to report serious adverse events suspected to be caused by medications, and are not even encouraged to report adverse events other than those classified as "serious." *See* Timothy Brewer, *Postmarketing Surveillance and Adverse Drug Reactions*, 281(9) JAMA 824 (Mar. 3, 1999). Doctors may not easily or immediately recognize a causal connection between a new drug and a deleterious side effect. Adverse events are thus significantly underreported; reported events are thought to represent only 1% to 10% of total complications. *See* A. S. Rogers et al., *Physician Knowledge, Attitudes, and Behavior Related to Reporting Adverse Drug Events*, 148(7) JAMA (July 1, 1988); Lots La Grenade et al., *Underreporting of Hemorrhagic Stroke Associated with Phenylpropanolamine*, 286 (24) JAMA

3081, 84-86 (Dec. 26, 2001); *see also* Making Health Care Safer: A Critical Analysis of Patient Safety Practices. Rockville, MD: Agency for Healthcare Research and Quality (K.G. Shojania et al., eds., 2001), at chap 4: Evidence Report/Technology Assessment No. 43, AHRQ publication 01-E058 (finding that only 1.5% of all adverse events result in an incident report, and only 6% of adverse drug events are identified properly).

In recent years, multiple drugs have been pulled off the market after new evidence of their lack of efficacy or increased safety concerns is revealed. *See, e.g.*, Alex Berenson, *Panel Doubts Two Drugs Used to Fight Cholesterol*, N.Y. Times, Mar. 31, 2008, at C1 (noting a two-year clinical trial of two widely prescribed cholesterol drugs showed the drugs did not slow arterial plaque growth; the drugs' initial FDA approval was based on short-term limited studies and not outcome trials). As one commentator noted,

> Perhaps the most terrifying aspect of the aforementioned "bad drug" cases [referring to Avandia, Vioxx, Fen-phen, Parlodel, DES, Ortho Evra, and Paxil] is not that negative or harmful side effects were ultimately linked to the drugs, but the amount of time the drugs remained on the market *without adequate warning to the consumers*, after the manufacturers knew (or had reason to know) of either the dangerous risks or the general ineffectiveness of the drugs.

Baswell, *supra,* at 1803 (original emphasis) (arguing that the FDA should require drug companies to provide all scientifically supported interpretations to doctors and consumers so that consumers may make a truly educated choice); *see, e.g.*, Gardiner Harris, *Heart Surgery Drug Pulled from Market: Bayer, Under Pressure, Acts After New Signs of a Fatality Risk*, N.Y. Times, Nov. 6, 2007, at A35 (reporting on Bayer's withdrawal of its drug Trasylol after a study suggested it increased death rates); Gardiner Harris & Alex Berenson, *Drug Companies Near an Old Goal* N.Y. Times, Apr. 6, 2008 (reporting on the Ortho Evra birth control patch lawsuit

against Johnson & Johnson based on allegations the company concealed research showing safety dangers for six years, delaying the eventual imposition of an FDA label change).

In part, delays in drug withdrawals are built into our pharmaceutical industry as it is currently structured and regulated.

> [O]nce a drug is approved, halting its sales is extremely difficult. Experts on [FDA] advisory panels are often loath to take widely used medicines out of doctors' hands, even when their safety is uncertain. This history also shows how vulnerable the F.D.A.'s drug approval system can be to unwelcome surprises.

Harris, *Heart Surgery Drug*, *supra*.

VI. FDA Approval and Regulation of Zyprexa

Plaintiffs' claims for overpricing span a period of twelve years, from Zyprexa's approval in 1996 to the present. The summary below of Zyprexa-related events that occurred during that time is by no means a complete account of what actually happened or what is reflected in the millions of documents produced by Lilly during discovery. Some of the information has already been discussed in this court's prior Zyprexa opinions.

A. Pre-Approval Studies

In the early 1990s, Lilly began seeking FDA approval of olanzapine for use in treatment of psychotic disorders. Before applying for FDA approval of Zyprexa for treatment of schizophrenia in 1996, Lilly performed a variety of studies to test the drug's safety and efficacy. Early studies revealed Zyprexa was associated with weight gain. Lilly's 1993 HGAV study reported that "weight gain was evident and uniform in all subjects, with an average gain of nearly 9 pounds." Jason A. Plassard, & Brian D. Beato, Olanzapine in Human Plasma, Final Report, Lilly Study FID-LC-HGAV (Nov. 1993), at 48. Statistical analysis of HGAV data performed in

April 1995 noted that "weight gain was evident and uniform in all subjects, with an average gain of nearly 9 pounds over the study duration," or approximately one and a half pounds per week. *Id.* at 47.

In August 1995, in the "Olanzapine Integrated Summary of Safety" report prepared for submission to the FDA, which included data from 3139 patients involved in approximately fifty worldwide olanzapine studies, Lilly noted that nearly 30% of patients on olanzapine in those trials reported incidences of weight gain. Olanzapine Integrated Summary of Safety: Psychosis, Lilly Research Laboratories, Aug. 31, 1995, at 111; *see* Wirshing Decl. 36. Compared with Haldol, an FGA, weight gain occurred more frequently in patients treated with Zyprexa. Olanzapine Integrated Summary of Safety at 166 ("A potentially clinically significant weight gain (≥7% from baseline) was experienced by 20.3% of olanzapine-treated patients compared with 5.0% of haloperidol patients.").

B. Initial Approval for Schizophrenia

Lilly was not required to, and did not, show that Zyprexa was better than, or even as good as, existing antipsychotics, or that it was safer or had fewer side effects than drugs already available to treat psychotic disorders. In seeking FDA approval, Lilly relied on two controlled studies showing Zyprexa to be superior to a placebo in the management of the symptoms of psychotic disorders in patients with schizophrenia during short-term, six-week-long studies. News Release, Lilly's Zyprexa (olanzapine) Cleared for Marketing for Treatment of Psychotic Disorders, Eli Lilly & Co., Oct. 1, 1996, at 2 [hereinafter Lilly News Release, Oct. 1, 1996]. "[F]or a drug anticipated to be used for lifetime treatment of an incurable disease, only 301 patients received at least 1 year of treatment while only 876 received at least 6 months of

treatment." Wirshing Decl. 36 (citing C.M. Beasley et al., *Efficacy of Olanzapine: An Overview of Pivotal Clinical Trials*, 58 J. Clin. Psychiatry 7-12 (1997)).

Before approving Zyprexa, the FDA expressed some concerns about both the long-term effectiveness and Lilly's claims of the comparative efficacy of Zyprexa. While Dr. Paul Leber, M.D., Director of the FDA's Division of Neuropharmacological Drug Products, had no reservations about the FDA review team's unanimous recommendation to approve Zyprexa, he "d[id] have a number of observations about olanzapine and the sponsor's development program that are of potential importance in regard to the kind of promotional claims that it may or may not be appropriate to allow Lilly to advance for Zyprexa." Leber Memo 2, Zyprexa NDA File, Aug. 18, 1996. With respect to long-term effectiveness, Dr. Leber noted that:

> The evidence adduced in the sponsor's short term (nominally 6 week long) studies, although it unquestionably provides compelling proof *in principle* of olanzapine's acute antipsychotic action, does not, because of 1) the highly selected nature of the patients admitted to study, 2) the high incidence of censored observations in the controlled trials, and 3) the indirect means used to assess the product's antipsychotic effects, provide a useful quantitative estimate of how effective (even in the short run) olanzapine actually will be in the population for whom it is likely to be prescribed upon marketing.
>
> The relatively short duration of the controlled clinical trials the sponsor relies upon, as might be anticipated, leaves us largely uninformed both about how effective a "maintenance" treatment olanzapine will be in extended use, and how best to administer it (i.e., dose and regimen) for that use.

Id. at 2-3 (emphasis in original) (footnote omitted).

As to comparative efficacy claims, Dr. Leber believed "the data adduced in the Zyprexa NDA is . . . insufficient to permit the sponsor to make claims asserting the product's superiority to haloperidol [Haldol, an FGA]." *Id.* at 5. While offering criticisms of some of the studies offered in support of the assertion, Dr. Leber specifically noted: